

STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 133847

TO: Rei-Tsang Shiao
Location: 5a10 / 5c18
Wednesday, September 29, 2004
Art Unit: 1626
Phone: 272-0707
Serial Number: 10 / 692856

From: Jan Delaval
Location: Biotech-Chem Library
Rem 1A51
Phone: 272-2504

jan.delaval@uspto.gov

Search Notes

Access DB# 133547

Jan Delgado
for search

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Robert (Robt) Shiao Examiner #: 79521 Date: 9/28/04
Art Unit: 1626 Phone Number: 2-0707 Serial Number: 10/692856
Mail Box and Bldg/Room Location: 5A10/5c18 Results/Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

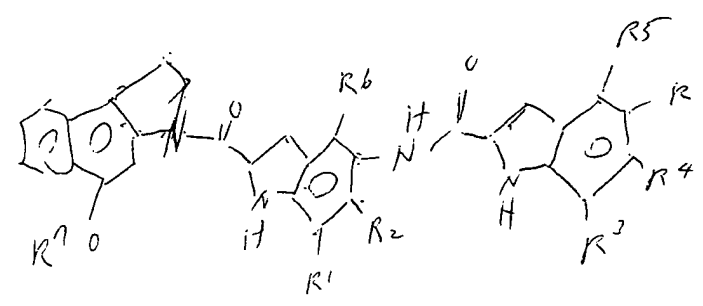
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc. if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: prodrugs of cc-1065
Inventors (please provide full names): Xiongxin

Earliest Priority Filing Date: _____

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

*I search a cpd I of female (I) & linked
to female (V).*



*R, R1 ~ R7
are sub.*

*ci method of use of cpd I
the sub cpd of claim 18*

STAFF USE ONLY		Type of Search	Vendors and cost where applicable
Searcher: <u>an</u>	NA Sequence (#) _____	STN <u>✓</u>	
Searcher Phone #: <u>22504</u>	AA Sequence (#) _____	Dialog _____	
Searcher Location: _____	Structure (#) <u>✓</u>	Questel/Orbit _____	
Date Searcher Picked Up: <u>9/19</u>	Bibliographic _____	Dr.Link _____	
Date Completed: <u>9/29</u>	Litigation _____	Lexis/Nexis _____	
Searcher Prep & Review Time: _____	Fulltext _____	Sequence Systems _____	
Clerical Prep Time: <u>15</u>	Patent Family _____	WWW/Internet _____	
Online Time: <u>+25</u>	Other _____	Other (specify) _____	

=> fil reg

FILE 'REGISTRY' ENTERED AT 15:55:39 ON 29 SEP 2004

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 28 SEP 2004 HIGHEST RN 753424-73-6

DICTIONARY FILE UPDATES: 28 SEP 2004 HIGHEST RN 753424-73-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

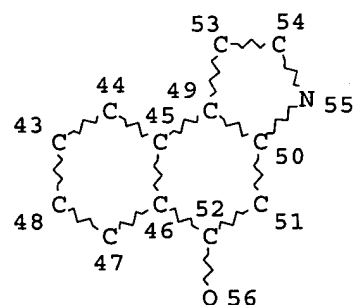
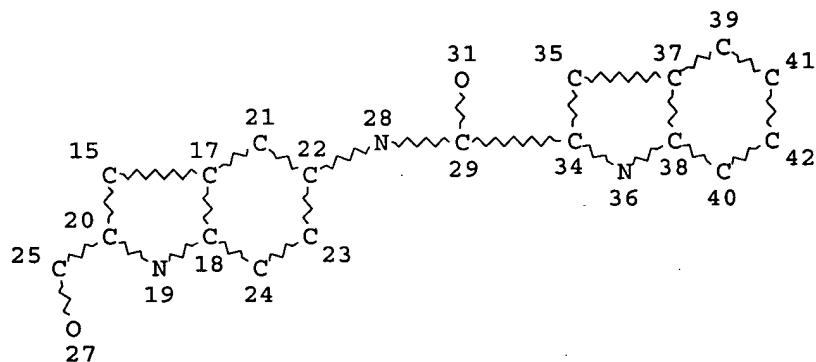
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d sta que 125

L1 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

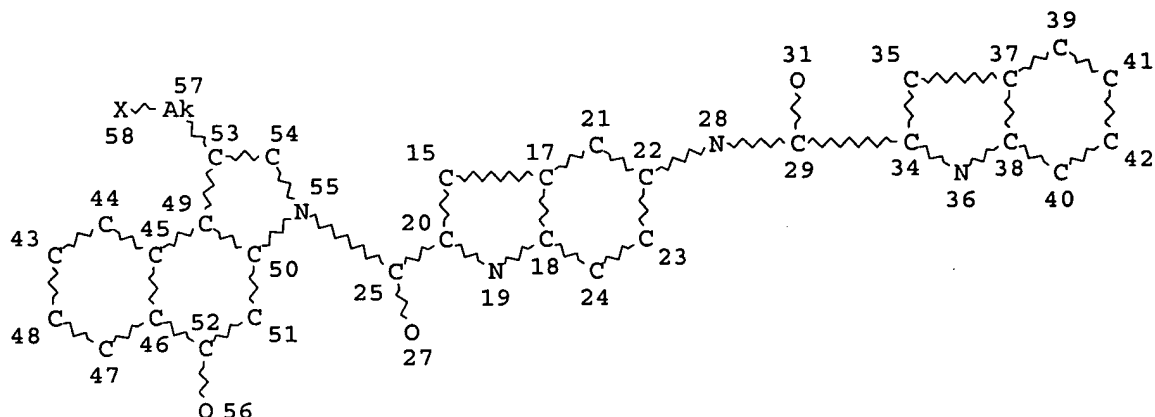
GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 37

STEREO ATTRIBUTES: NONE

L5 116 SEA FILE=REGISTRY SSS FUL L1
L24 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 41 22 55
NUMBER OF NODES IS 39

STEREO ATTRIBUTES: NONE
L25 97 SEA FILE=REGISTRY SUB=L5 SSS FUL L24

100.0% PROCESSED 98 ITERATIONS
SEARCH TIME: 00.00.01

97 ANSWERS

=> d his

(FILE 'HOME' ENTERED AT 15:35:49 ON 29 SEP 2004)
SET COST OFF

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L2 4 S L1
L3 STR L1
L4 3 S L3
L5 116 S L1 FUL
SAV TEMP L5 SHIAO692/A
L6 STR L1
L7 97 S L6 FUL SUB=L5
SAV L7 SHIAL692A/A TEMP

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L8 25 S L7
L9 32 S L5
L10 32 S L8,L9
L11 3 S L10 AND (CHARI R? OR YONGXIN R?)/AU
L12 1 S L10 AND ZHAO R?/AU
L13 3 S L10 AND IMMUNOGEN?/PA,CS
L14 3 S L11-L13
SEL HIT RN

FILE 'REGISTRY' ENTERED AT 15:43:59 ON 29 SEP 2004

L1 116 S L1 FUL

L16 10 S L15 AND 7/NR
 L17 4 S L15 AND NC2NC2/ES
 L18 2 S L17 NOT 9/O
 L19 4 S L16 AND (C35H30CLN5O4S2 OR C34H28CLN5O4S OR C35H31CLN5O7PS2 O
 L20 5 S L15 AND 9/NR
 L21 2 S L20 NOT (9/O OR P/ELS)
 L22 8 S L18,L19,L21
 SEL MF
 L23 8 S E21-E28 AND L5
 L24 STR L6
 L25 97 S L24 FUL SUB=L5
 SAV TEMP L25 SHIAO692B/A
 L26 89 S L25 NOT L22

FILE 'HCAOLD' ENTERED AT 15:52:55 ON 29 SEP 2004

L27 0 S L22
 L28 0 S L26

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L29 3 S L22
 L30 24 S L26
 L31 20 S L30 AND (PD<=20020405 OR PRD<=20020405 OR AD<=20020405)
 L32 3 S L29 AND (ZHAO R? OR YONGXIN ? OR CHARI ?)/AU
 L33 3 S L29 AND IMMUNOGEN?/PA,CS
 L34 3 S L29,L32,L33

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 L36 12 S L26
 L37 12 S L35,L36

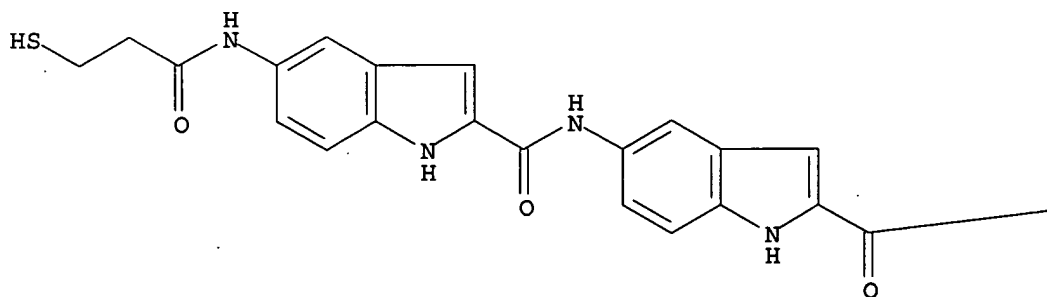
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=> d ide can tot l22

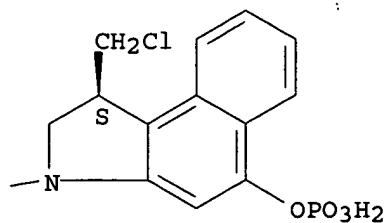
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 RN 615538-48-2 REGISTRY
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 FS STEREOSEARCH
 MF C34 H29 Cl N5 O7 P S
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
 DT.CA CAplus document type: Patent
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

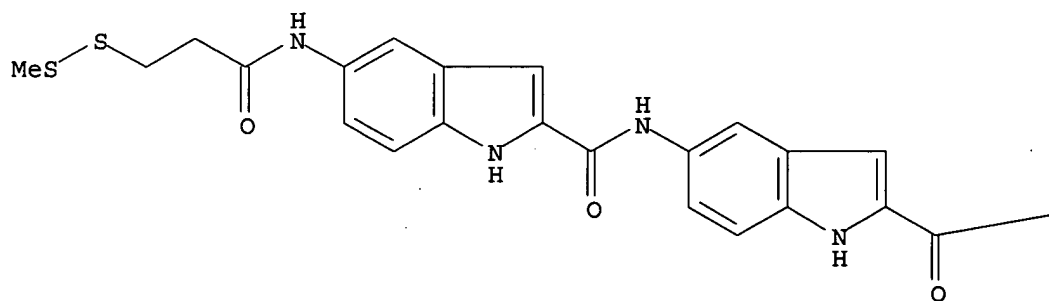
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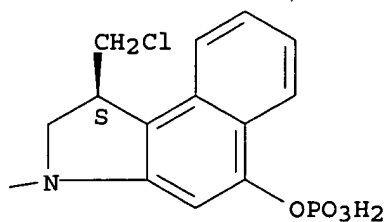
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 MF C35 H31 Cl N5 O7 P S2
 SR CA
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 DT.CA CAPLUS document type: Patent
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.

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PAGE 1-B



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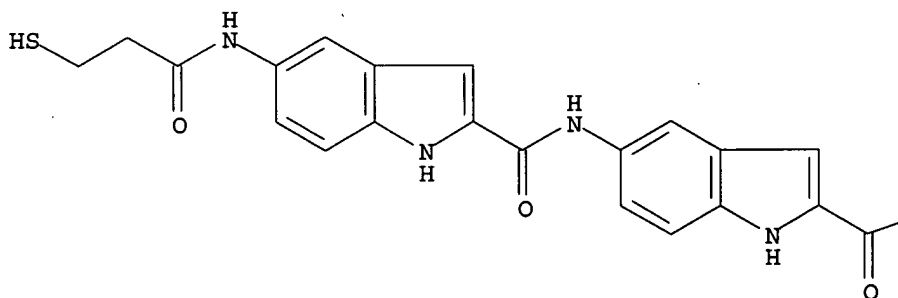
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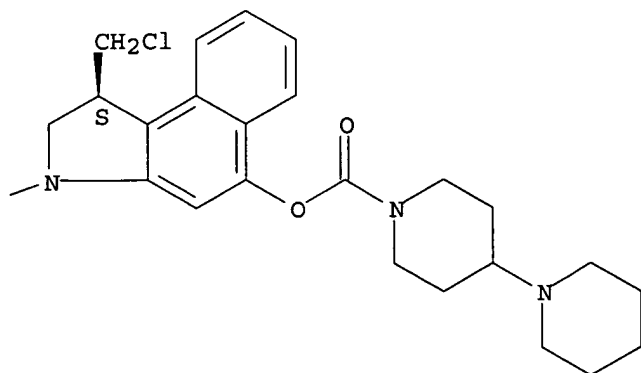
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RN 615538-46-0 REGISTRY
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FS STEREOSEARCH
MF C45 H46 Cl N7 O5 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA Caplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

Absolute stereochemistry.

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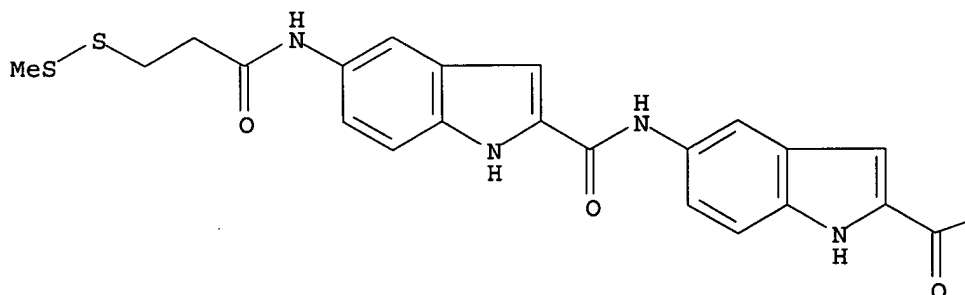
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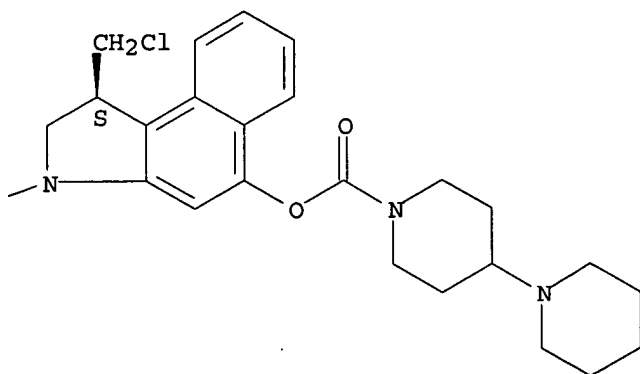
L22 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615538-45-9 REGISTRY
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (1S)-1-(chloromethyl)-2,3-dihydro-3-[[[5-[[[5-[[3-(methylthio)-1-oxopropyl]amino]-1H-indol-2-yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl ester (9CI) (CA INDEX NAME)
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MF C46 H48 Cl N7 O5 S2
SR CA
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DT.CA Caplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.

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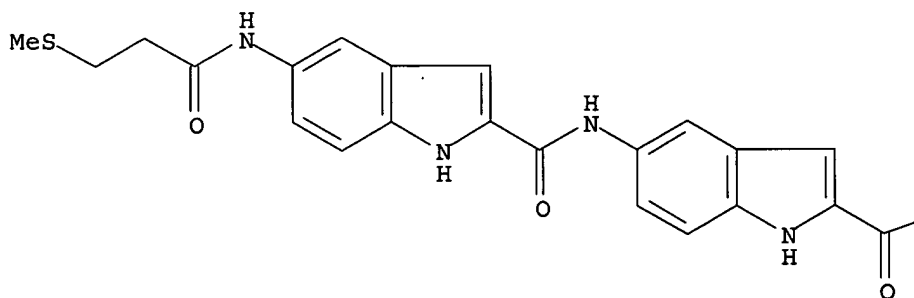
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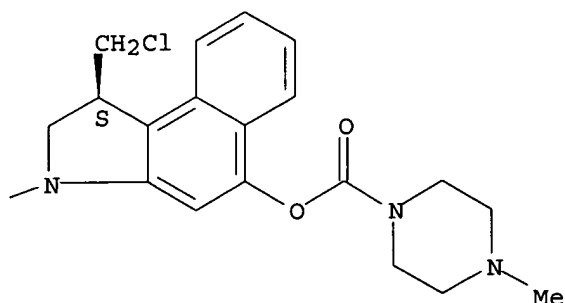
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RN 615538-44-8 REGISTRY
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(9CI) (CA INDEX NAME)
FS STEREOSEARCH
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SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA CAPLUS document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP
(Properties); USES (Uses)

Absolute stereochemistry.

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1 REFERENCES IN FILE CA (1907 TO DATE)
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REFERENCE 1: 139:341741

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RN 615538-42-6 REGISTRY
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yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl ester
(9CI) (CA INDEX NAME)
FS STEREOSEARCH

MF C41 H40 Cl N7 O5 S2

SR CA

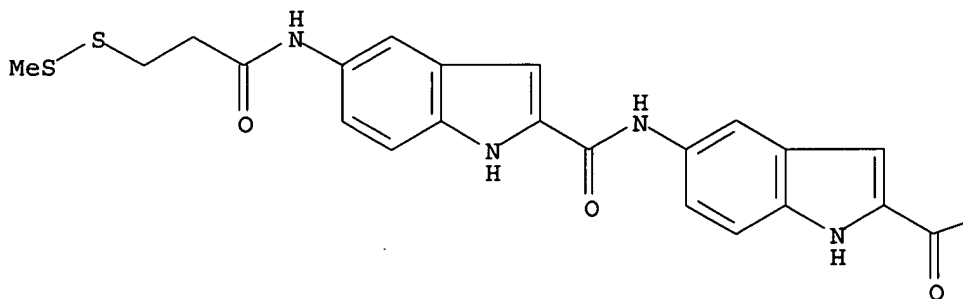
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DT.CA Caplus document type: Patent

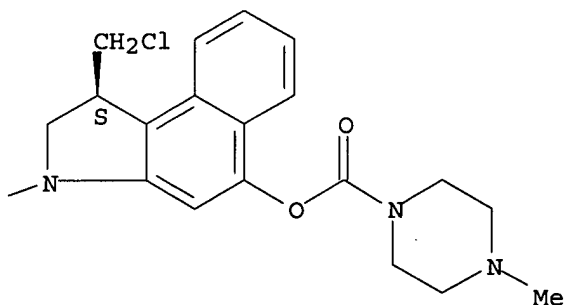
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.

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PAGE 1-B



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1 REFERENCES IN FILE CA (1907 TO DATE)

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REFERENCE 1: 139:341741

L22 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2004 ACS on STN

RN 501666-85-9 REGISTRY

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FS STEREOSEARCH

MF C35 H30 Cl N5 O4 S2

SR CA

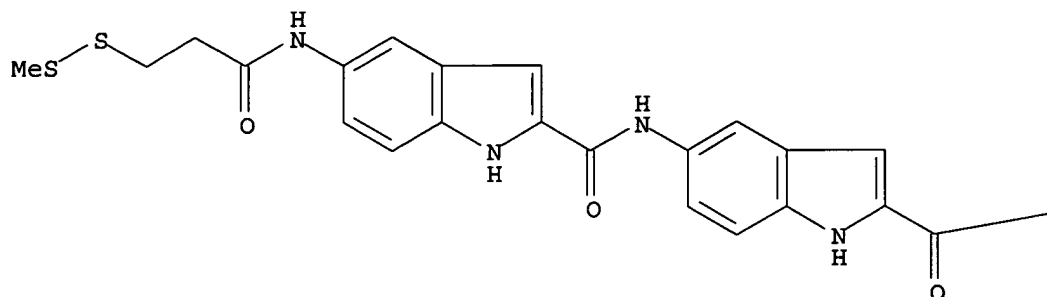
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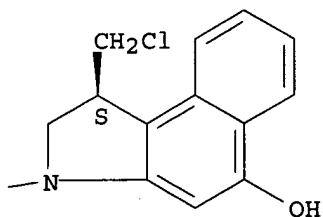
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.

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PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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REFERENCE 1: 139:341741

REFERENCE 2: 138:238007

L22 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2004 ACS on STN

RN 169901-27-3 REGISTRY

CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[(3-mercapto-1-oxopropyl)amino]-, (S)-(9CI) (CA INDEX NAME)

FS STEREOSEARCH

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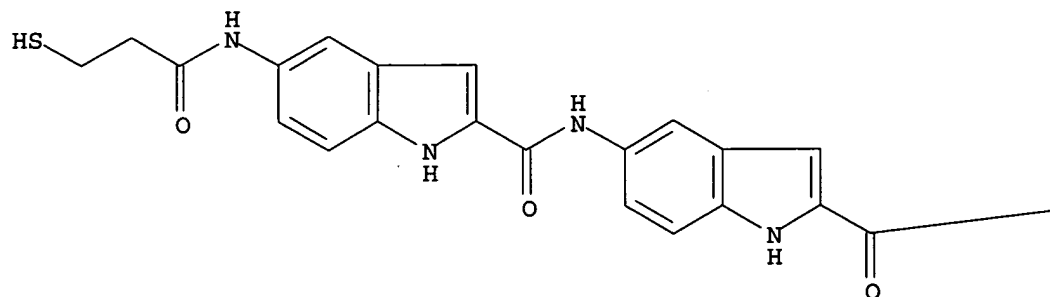
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DT.CA Caplus document type: Journal

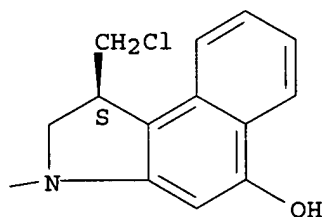
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 1 REFERENCES IN FILE CA (1907 TO DATE)
- 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
- 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 123:306084

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FILE 'HCAPLUS' ENTERED AT 15:56:07 ON 29 SEP 2004

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FILE COVERS 1907 - 29 Sep 2004 VOL 141 ISS 14

FILE LAST UPDATED: 28 Sep 2004 (20040928/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d 134 all hitstr tot

L34 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2003:836793 HCAPLUS
 DN 139:341741
 ED Entered STN: 24 Oct 2003
 TI Improved prodrugs of CC-1065 analogs
 IN Zhao, Robert Yongxin; Chari, Ravi V. J.
 PA Immunogen, Inc., USA
 SO PCT Int. Appl., 50 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K
 CC 63-6 (Pharmaceuticals)
 Section cross-reference(s): 1, 26

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003086318	A2	20031023	WO 2003-US7282	20030320
	WO 2003086318	A3	20040325		
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	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	US 2003199519	A1	20031023	US 2002-116053	20020405
	US 6756397	B2	20040629		
	US 2004109867	A1	20040610	US 2003-692856	20031027
PRAI	US 2002-116053	A	20020405		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003086318	ICM	A61K
US 2003199519	ECLA	A61K031/407; A61K031/4545; A61K031/496; A61K031/675; C07D209/60; C07F009/572V; C07F009/6558B
US 2004109867	ECLA	A61K031/407; C07D209/60; C07F009/572V; C07F009/6558B; A61K031/4545; A61K031/496; A61K031/675

AB Prodrugs of analogs of the antitumor antibiotic CC-1065 are described, comprising both (i) a cleavable protective group, such as a piperazino carbamate, a 4-piperidino-piperidino carbamate or a phosphate, in which the protecting group confers enhanced water solubility and stability upon the prodrug, and (ii) a moiety, such as a disulfide, that can conjugate to a cell binding reagent, e.g., an antibody. The therapeutic use of such prodrug conjugates is also described. These prodrugs of cytotoxic agents have therapeutic use because they can deliver cytotoxic prodrugs to a specific cell population for enzymic conversion to cytotoxic drugs in a targeted fashion.

ST antibiotic CC1065 analog prodrug prepn tumor targeting

IT Antibodies and Immunoglobulins
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cell binding agents; preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

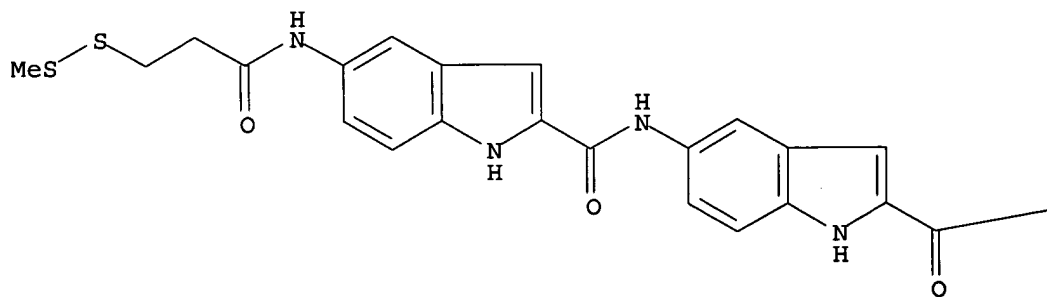
IT Drug delivery systems
 (conjugates of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT Antitumor agents
 Neoplasm

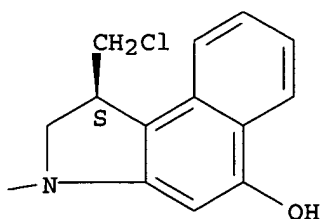
- (preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
- IT Drug delivery systems
(prodrugs; preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
- IT 501441-05-0P 501666-85-9P 615538-42-6P
615538-45-9P 615538-47-1P 615538-49-3P
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(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
- IT 615538-44-8P 615538-46-0P 615538-48-2P
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(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
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RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
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RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
- IT 615538-53-9P 615538-54-0P 615538-55-1P 615538-56-2P 615538-57-3DP, salt 615538-58-4P 615538-59-5DP, salt
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
- IT 501666-85-9P 615538-42-6P 615538-45-9P 615538-47-1P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)
- RN 501666-85-9 HCAPLUS
- CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[[3-(methylthio)-1-oxopropyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

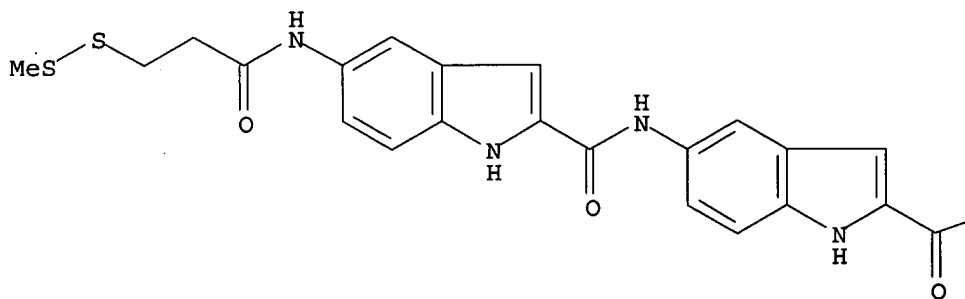


RN 615538-42-6 HCAPLUS

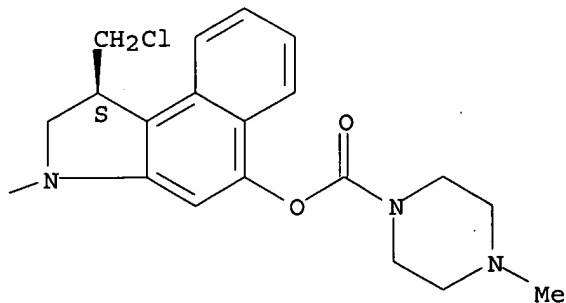
CN 1-Piperazinecarboxylic acid, 4-methyl-, (1S)-1-(chloromethyl)-2,3-dihydro-3-[[[5-[[[5-[[3-(methyldithio)-1-oxopropyl]amino]-1H-indol-2-yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

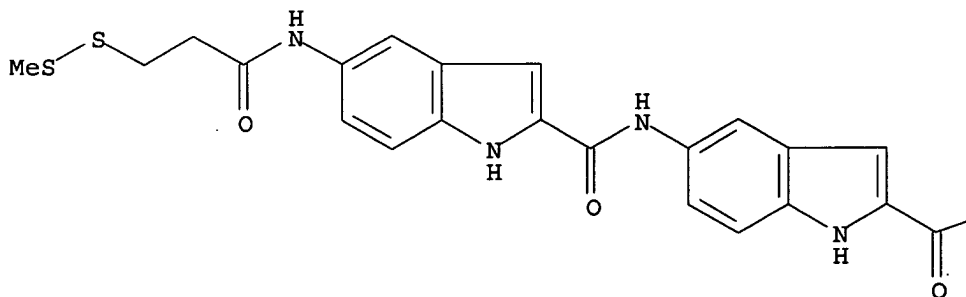


RN 615538-45-9 HCAPLUS

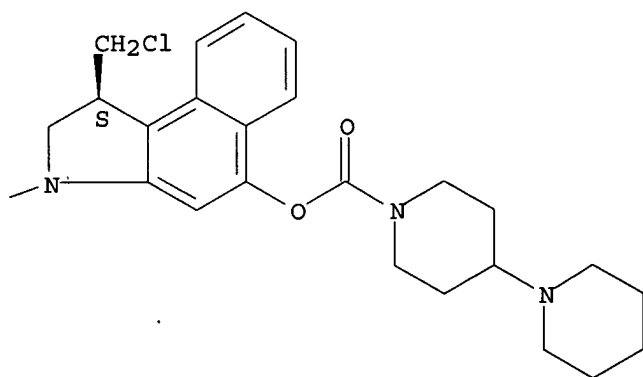
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (1S)-1-(chloromethyl)-2,3-dihydro-3-[[[5-[[[5-[[3-(methyldithio)-1-oxopropyl]amino]-1H-indol-2-yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

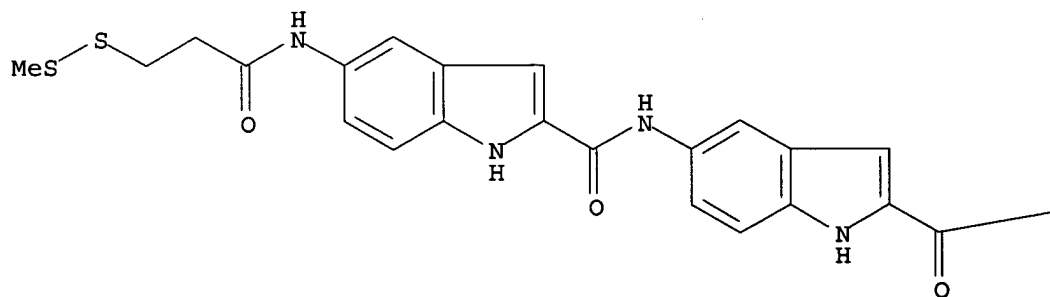


RN 615538-47-1 HCAPLUS

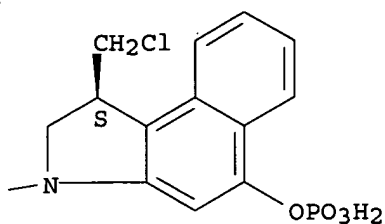
CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-(phosphonooxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[[3-(methylthio)-1-oxopropyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT 615538-44-8P 615538-46-0P 615538-48-2P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)

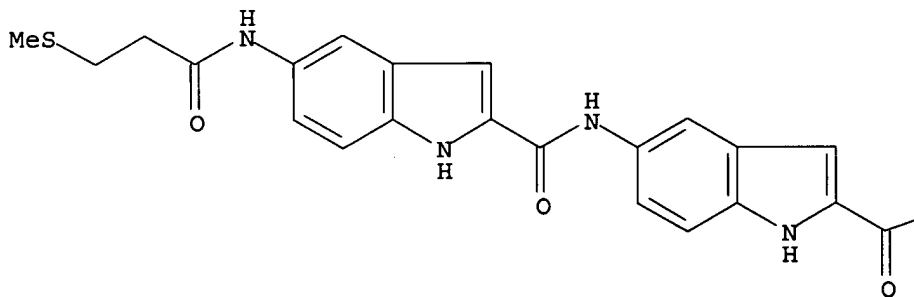
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

RN 615538-44-8 HCAPLUS

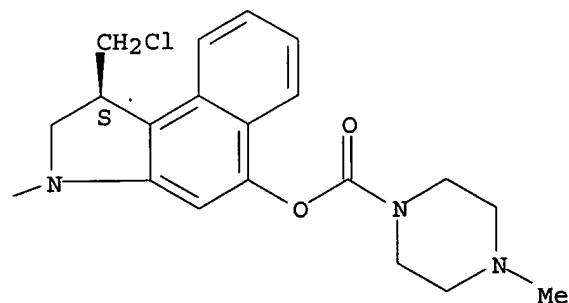
CN 1-Piperazinecarboxylic acid, 4-methyl-, (1S)-1-(chloromethyl)-2,3-dihydro-
3-[[5-[[[5-[[3-(methylthio)-1-oxopropyl]amino]-1H-indol-2-yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl ester
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

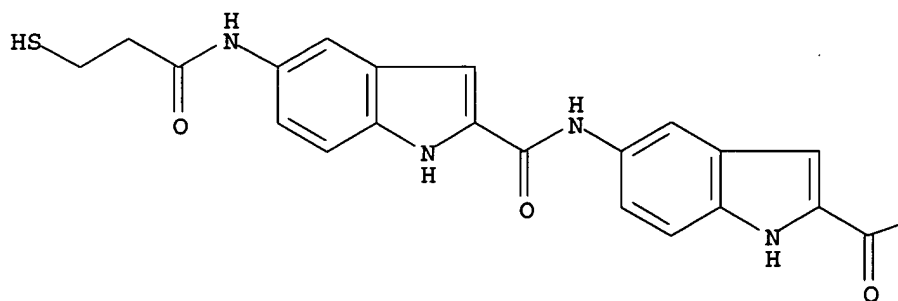


RN 615538-46-0 HCAPLUS

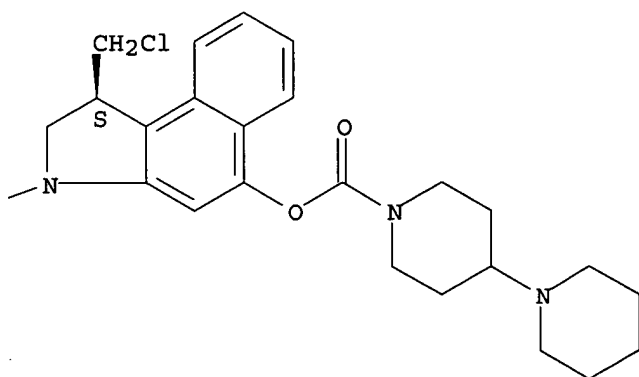
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (1S)-1-(chloromethyl)-2,3-dihydro-
3-[[5-[[[5-[[3-mercapto-1-oxopropyl]amino]-1H-indol-2-yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

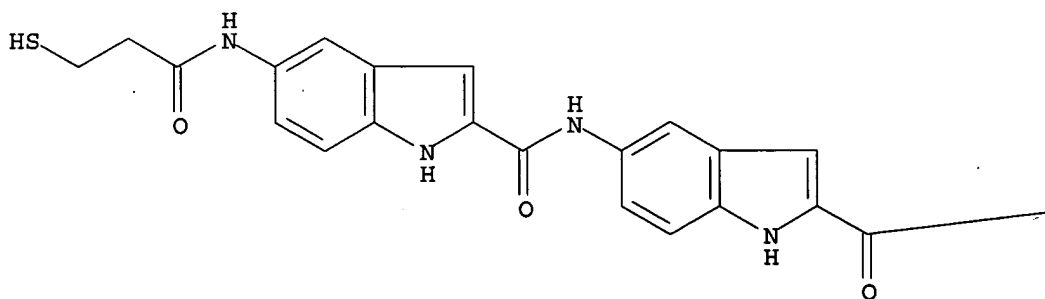


RN 615538-48-2 HCAPLUS

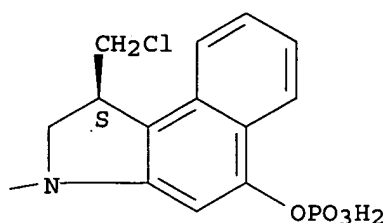
CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-(phosphonooxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[(3-mercapto-1-oxopropyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L34 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2003:217996 HCAPLUS
 DN 138:238007
 ED Entered STN: 20 Mar 2003
 TI Improved synthesis of (-)-5-hydroxy-1(S)-chloromethyl-1,2-dihydro-3H-benz[e]indole, an intermediate in the preparation of CC-1065 analogs
 IN Yongxin, Robert; Chari, Ravi V. J.
 PA Immunogen, Inc., USA
 SO U.S., 15 pp.
 CODEN: USXXAM
 DT Patent
 LA English
 IC ICM C07D209-56
 NCL 548450000
 CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6534660	B1	20030318	US 2002-116052	20020405
	US 6586618	B1	20030701	US 2002-265329	20021007
	US 2003195365	A1	20031016	US 2002-265452	20021007
	WO 2003087055	A1	20031023	WO 2003-US7276	20030319
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRAI US 2002-116052 A3 20020405

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6534660	ICM	C07D209-56
	NCL	548450000
US 2003195365	ECLA	C07D209/60
OS	CASREACT 138:238007; MARPAT 138:238007	
GI		

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Disclosed is an improved synthesis of 5-hydroxy-1(S)-chloromethyl-1,2-

dihydro-3H-benz[e]indole [I; seco(-)CBI] comprising (a) protecting the hydroxy and amino groups of 1-hydroxy-3-naphthylamine with the same protecting group, (b) performing halogenation, alkylation, and ring closure reactions to provide the N,O-protected racemate of I, (c) isolating the (-)-isomer, and (d) removing the protecting groups. By using the same protecting group for the amino and hydroxy groups, this method eliminates redundant protection and deprotection steps, shortens synthesis time, improves product yield, and improves separation of enantiomers. Further disclosed is an improved syntheses of a wide variety of CC-1065 analogs that comprise a CBI alkylating moiety, such as the cell-targeted antitumor antibiotic DC1 and its derivs. For example, 1,3-dihydroxynaphthalene was aminated with NH₃ and converted to N-(tert-butoxycarbonyl)-1-(tert-butoxycarbonyloxy)-3-naphthylamine (69%) with (BOC)₂O in the presence of DIPEA in THF. Iodination with N-iodosuccinimide (86%), alkylation with (Z)-1,3-dichloropropene in the presence of NaH in DMF (93%), and ring closure using Bu₃SnH in the presence of AIBN in benzene (94%) gave the racemic N,O-protected benz[e]indole. The racemic mixture was separated using a chiral HPLC column eluting with 20% i-PrOH in hexane. Deprotection with HCl in the presence of Et₃SiH in EtOAc gave (-)-I•HCl in 90% purity. Two synthetic routes for conversion of (-)-I•HCl to DC1-SMe (II) are also provided.

ST stereoselective secoCBI prepn hydroxynaphthylamine alkylation cyclization;
benzindole intermediate CC1065 analog prepn

IT Alkylation
Cyclization

(preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT Protective groups

(tert-butoxycarbonyl; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT 501440-85-3P, 5-(tert-Butoxycarbonyloxy)-3-(tert-butoxycarbonyl)-1-(chloromethyl)-1,2-dihydro-3H-benz[e]indole

RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PYP (Physical process); PREP (Preparation); PROC (Process)

(intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT 501440-87-5P

RL: IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT 16730-20-4P, 5-Nitroindole-2-carboxylic acid 71086-99-2P, Ethyl

5-aminoindole-2-carboxylate 152213-42-8P, tert-Butyl

5-nitroindole-2-carboxylate 152213-43-9P, tert-Butyl

5-aminoindole-2-carboxylate 501440-80-8P 501440-82-0P 501440-84-2P,

2-[N-(tert-Butoxycarbonyl)-N-(3-chloro-2-propen-1-yl)amino]-4-(tert-butoxycarbonyloxy)-1-iodonaphthalene 501440-88-6P, tert-Butyl

5-[[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-carboxylate 501440-90-0P,

tert-Butyl 5-[[[(5-aminoindol-2-yl)carbonyl]amino]indole-2-carboxylate

501440-92-2P 501440-94-4P 501440-95-5P 501440-97-7P 501440-99-9P,

Ethyl 5-[[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-carboxylate

501441-01-6P, 5-[[[(5-Nitroindol-2-yl)carbonyl]amino]indole-2-carboxylic

acid 501441-05-0P, 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole

RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT 501440-86-4P

RL: BYP (Byproduct); PUR (Purification or recovery); PREP (Preparation)

(preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT 132-86-5, 1,3-Dihydroxynaphthalene 542-75-6, 1,3-Dichloropropene

16732-57-3, Ethyl 5-nitroindole-2-carboxylate 24424-99-5, Di-tert-butyl dicarbonate 68617-64-1, 3-(2-Pyridyldithio)propionic acid 138148-59-1
 RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT 130007-89-5P, 5-Hydroxy-1-(S)-((chloromethyl))-1,2-dihydro-3H-benz[e]indole hydrochloride 299411-68-0P, 5-Hydroxy-1-(S)-((chloromethyl))-1,2-dihydro-3H-benz[e]indole
 RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(target intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT 501666-85-9P 501666-87-1P
 RL: IMF (Industrial manufacture); PREP (Preparation)
 (target product; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Boger, D; Chem Rev 1997, V97, P787 HCAPLUS

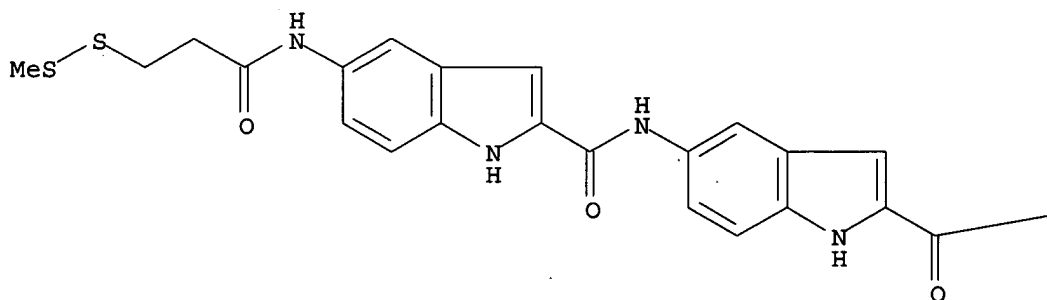
IT 501666-85-9P
 RL: IMF (Industrial manufacture); PREP (Preparation)
 (target product; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

RN 501666-85-9 HCAPLUS

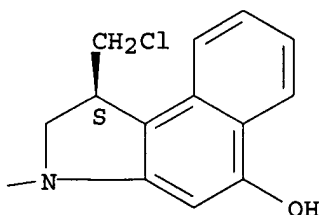
CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[[3-(methyldithio)-1-oxopropyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L34 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:809548 HCAPLUS

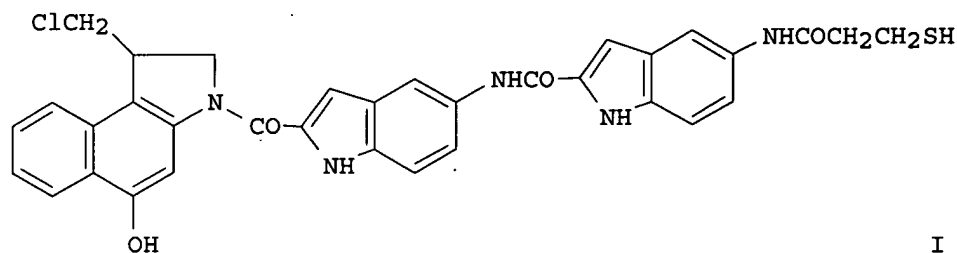
DN 123:306084

ED Entered STN: 23 Sep 1995

TI Enhancement of the selectivity and antitumor efficacy of a CC-1065 analog

through immunoconjugate formation

AU **Chari, Ravi V. J.**; Jackel, Kristine A.; Bourret, Lizabeth A.;
 Derr, Susan M.; Tadayoni, B. Mitra; Mattocks, Kristin M.; Shah, Sudhir A.;
 Liu, Changnian; Blattler, Walter A.; Goldmacher, Victor S.
 CS **ImmunoGen. Inc., Cambridge, MA, 02139-4239, USA**
 SO Cancer Research (1995), 55(18), 4079-84
 CODEN: CNREA8; ISSN: 0008-5472
 PB American Association for Cancer Research
 DT Journal
 LA English
 CC 1-6 (Pharmacology)
 Section cross-reference(s): 63
 GI

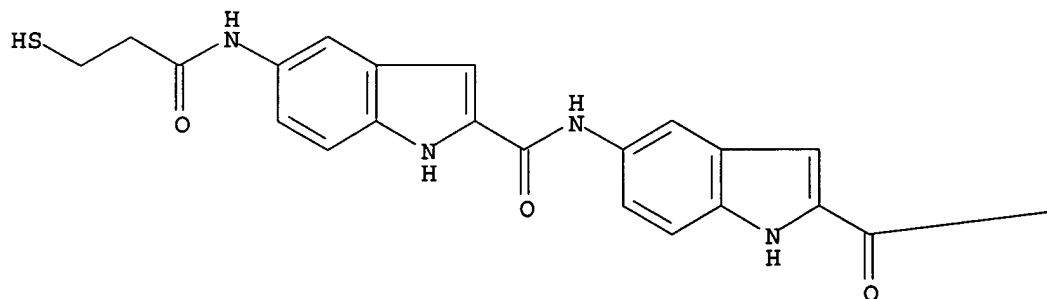


AB Bis-indolyl-(seco)-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one
 compds. are synthetic analogs of CC-1065 that are highly cytotoxic toward
 a broad spectrum of tumor cell lines. One of these compds., called DC1
 (I), was conjugated to antibodies via novel cleavable disulfide linkers.
 Conjugates of DC1 with murine mAbs anti-B4 and N901 directed against
 tumor-associated antigens CD19 and CD56, resp., proved to be extremely potent
 and antigen selective in killing target cells in culture. DC1 conjugates
 with humanized versions of anti-B4 and N901 antibodies were also
 constructed and demonstrated to be as cytotoxic and selective as the resp.
 murine antibody conjugates. The anti-B4-DC1 conjugate showed antitumor
 efficacy in an aggressive metastatic human B-cell lymphoma survival model
 in SCID mice and completely cured animals bearing large tumors.
 Anti-B4-DC1 was considerably more effective in this tumor model than
 doxorubicin, cyclophosphamide, etoposide, or vincristine at their maximum
 tolerated doses.
 ST metastasis inhibitor immunoconjugate CC1065 analog; antitumor
 indolylcyclopropabenzindolone deriv immunoconjugate
 IT Antigens
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)
 (CD19, tumor-associated; enhancement of selectivity and antitumor efficacy
 of CC-1065 analog through immunoconjugate formation)
 IT Antigens
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)
 (CD56, tumor-associated; enhancement of selectivity and antitumor efficacy
 of CC-1065 analog through immunoconjugate formation)
 IT Pharmaceutical dosage forms
 (immunoconjugates, enhancement of selectivity and antitumor efficacy of
 CC-1065 analog through immunoconjugate formation)
 IT Neoplasm inhibitors
 (metastasis, enhancement of selectivity and antitumor efficacy of
 CC-1065 analog through immunoconjugate formation)
 IT 169901-27-3D, conjugates with murine mAbs anti-B4 and N901
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (enhancement of selectivity and antitumor efficacy of CC-1065 analog

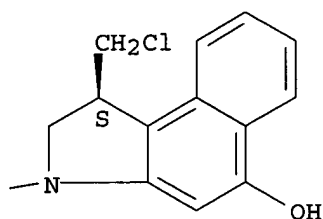
through immunoconjugate formation)
 IT 169901-27-3D, conjugates with murine mAbs anti-B4 and N901
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (enhancement of selectivity and antitumor efficacy of CC-1065 analog
 through immunoconjugate formation)
 RN 169901-27-3 HCAPLUS
 CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[(3-mercapto-1-oxopropyl)amino]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



=> d l31 all hitrn fhitstr tot

L31 ANSWER 1 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2003:836793 HCAPLUS
 DN 139:341741
 ED Entered STN: 24 Oct 2003
 TI Improved prodrugs of CC-1065 analogs
 IN Zhao, Robert Yongxin; Chari, Ravi V. J.
 PA Immunogen, Inc., USA
 SO PCT Int. Appl., 50 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K
 CC 63-6 (Pharmaceuticals)
 Section cross-reference(s): 1, 26

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003086318	A2	20031023	WO 2003-US7282	20030320 <--
	WO 2003086318	A3	20040325		

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1 structure
 displayed per
 reference
 see pages 85-end
 for all hits

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
 PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
 TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ,
 MD, RU, TJ, TM
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 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
 NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
 GW, ML, MR, NE, SN, TD, TG

US 2003199519 A1 20031023 US 2002-116053 20020405 <--
 US 6756397 B2 20040629
 US 2004109867 A1 20040610 US 2003-692856 20031027 <--
 PRAI US 2002-116053 A 20020405 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003086318	ICM	A61K
US 2003199519	ECLA	A61K031/407; A61K031/4545; A61K031/496; A61K031/675; C07D209/60; C07F009/572V; C07F009/6558B <--
US 2004109867	ECLA	A61K031/407; C07D209/60; C07F009/572V; C07F009/6558B; A61K031/4545; A61K031/496; A61K031/675 <--
AB	Prodrugs of analogs of the antitumor antibiotic CC-1065 are described, comprising both (i) a cleavable protective group, such as a piperazino carbamate, a 4-piperidino-piperidino carbamate or a phosphate, in which the protecting group confers enhanced water solubility and stability upon the prodrug, and (ii) a moiety, such as a disulfide, that can conjugate to a cell binding reagent, e.g., an antibody. The therapeutic use of such prodrug conjugates is also described. These prodrugs of cytotoxic agents have therapeutic use because they can deliver cytotoxic prodrugs to a specific cell population for enzymic conversion to cytotoxic drugs in a targeted fashion.	
ST	antibiotic CC1065 analog prodrug prepn tumor targeting	
IT	Antibodies and Immunoglobulins	
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (cell binding agents; preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)	
IT	Drug delivery systems (conjugates of prodrugs of antibiotic CC-1065 analogs for tumor targeting)	
IT	Antitumor agents Neoplasm (preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)	
IT	Drug delivery systems (prodrugs; preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)	
IT	501441-05-0P 501666-85-9P 615538-42-6P 615538-45-9P 615538-47-1P 615538-49-3P RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)	
IT	615538-44-8P 615538-46-0P 615538-48-2P RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)	
IT	92-54-6 4897-50-1, 4-Piperidino-piperidine 7693-46-1, 4-Nitrophenyl chloroformate 10025-87-3, Phosphoric trichloride 17176-77-1, Dibenzylphosphite 51805-45-9, Tris-(2-carboxyethyl) phosphine hydrochloride 138148-59-1 501441-01-6 564476-35-3 615538-50-6 RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)	
IT	615538-51-7P 615538-52-8P	

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
USES (Uses)

(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT 615538-53-9P 615538-54-0P 615538-55-1P
615538-56-2P 615538-57-3DP, salt 615538-58-4P
615538-59-5DP, salt

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT 501441-05-0P 615538-49-3P

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT 615538-51-7P 615538-52-8P

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT 615538-53-9P 615538-54-0P 615538-55-1P
615538-56-2P 615538-57-3DP, salt 615538-58-4P
615538-59-5DP, salt

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT 501441-05-0P

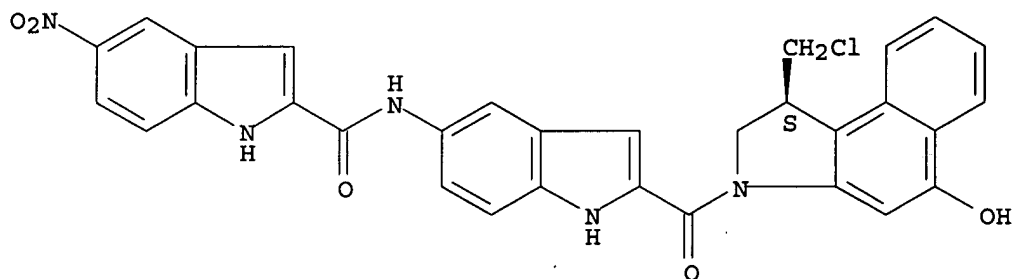
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

RN 501441-05-0 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:221652 HCAPLUS

DN 138:255007

ED Entered STN: 21 Mar 2003

TI Preparation of CBI analogues of CC 1065 and the duocarmycins for therapeutic use as anticancer agents

IN Boger, Dale L.

PA The Scripps Research Institute, USA

SO PCT Int. Appl., 35 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07D
 CC 26-6 (Biomolecules and Their Synthetic Analogs)
 Section cross-reference(s): 1, 63

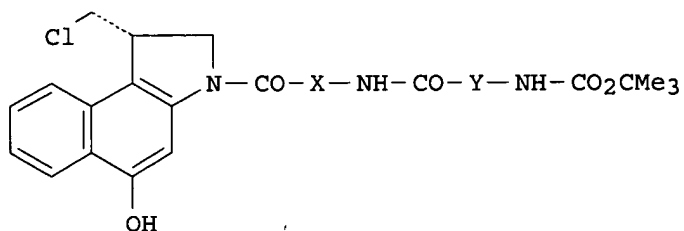
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003022806	A2	20030320	WO 2002-US28749	20020909 <--
	WO 2003022806	A3	20031113		
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	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	EP 1423110	A2	20040602	EP 2002-798201	20020909 <--
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PRAI	US 2001-318179P	P	20010907	<--	
	WO 2002-US28749	W	20020909		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003022806	ICM	C07D

OS MARPAT 138:255007
 GI



AB 132 CBI analogs I [X, Y = arylene, heteroarylene] of CC 1065 and the duocarmycins having dimeric monocyclic, bicyclic, and tricyclic heteroaroms. substituents were synthesized by a parallel route. The resultant analogs were evaluated with respect to their catalytic and cytotoxic activities. The relative contribution of the various dimeric monocyclic, bicyclic, and tricyclic heteroaroms. substituents within the DNA binding domain were characterized. Several of the resultant CBI analogs of CC 1065 and the duocarmycins were characterized as having enhanced catalytic and cytotoxic activities and were identified as having utility as anti-cancer agents. Thus, I (X = Y = -4-C6H4-) was prepared starting from 4-H2NC6H4CO2H and the hydrochloride salt of seco-CBI.

ST duocarmycin analog library prepn antitumor agent; CC1065 analog library prepn antitumor agent

IT DNA

RL: BSU (Biological study, unclassified); BIOL (Biological study) (alkylation; synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

- IT Alkylating agents, biological
Antitumor agents
Combinatorial library
Human
(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one
analogs of CC-1065 and the duocarmycins defining the contribution of
the DNA-binding domain)
- IT Neoplasm
(treatment; synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]i
ndol-4-one analogs of CC-1065 and the duocarmycins defining the
contribution of the DNA-binding domain)
- IT 69866-21-3DP, CC 1065, analogs 118292-34-5DP, Duocarmycin A, analogs
128300-14-1DP, (+)-CBI-CDPI, analogs 130288-24-3DP, (+)-Duocarmycin SA,
analogs 166104-33-2DP, (+)-CBI-CDPBI, analogs 166104-36-5DP,
(+)-CBI-CDPBO, analogs 372953-14-5P 372953-15-6P 372953-16-7P
372953-17-8P 372953-18-9P 372953-19-0P 372953-20-3P 372953-21-4P
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372953-27-0P 372953-28-1P 372953-29-2P 372953-30-5P 372953-31-6P
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372953-47-4P 372953-48-5P 372953-49-6P 372953-50-9P 372953-51-0P
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372953-73-6P 372953-74-7P 372953-75-8P 372953-76-9P 372953-77-0P
372953-78-1P 372953-79-2P 372953-80-5P 372953-81-6P 372953-82-7P
372953-83-8P 372953-84-9P 372953-85-0P 372953-86-1P 372953-87-2P
372953-88-3P 372953-89-4P 372953-90-7P 372953-91-8P 372953-92-9P
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372954-04-6P 372954-05-7P 372954-06-8P 372954-07-9P 372954-08-0P
372954-09-1P 372954-10-4P 372954-11-5P 372954-12-6P 372954-13-7P
372954-14-8P 372954-15-9P 372954-16-0P 372954-17-1P 372954-18-2P
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372954-39-7P 372954-40-0P 372954-41-1P 372954-42-2P 372954-43-3P
372954-44-4P 372954-45-5P 372954-46-6P 372954-47-7P 372954-48-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one
analogs of CC-1065 and the duocarmycins defining the contribution of
the DNA-binding domain)
- IT 99-05-8, 3-Aminobenzoic acid 150-13-0, 4-Aminobenzoic acid 40283-41-8,
2-Amino-4-thiazolecarboxylic acid 42933-44-8 45776-13-4 55341-87-2,
3-Amino-2-thiophenecarboxylic acid 82221-08-7 98589-46-9
130007-89-5, Seco-CBI hydrochloride 152213-40-6 263710-28-7
372953-12-3 372953-13-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one
analogs of CC-1065 and the duocarmycins defining the contribution of
the DNA-binding domain)
- IT 120506-51-6P 126092-98-6P 138730-83-3P 180258-47-3P 292070-82-7P
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502170-48-1P 502170-49-2P 502170-50-5P 502170-51-6P 502170-52-7P
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502170-64-1P 502170-66-3P 502170-68-5P 502170-70-9P 502170-72-1P
502170-74-3P 502170-76-5P 502170-79-8P 502170-81-2P 502170-83-4P
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502172-10-3P	502172-12-5P	502172-14-7P	502172-16-9P	502172-18-1P
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

IT 372954-24-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

IT 372954-24-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

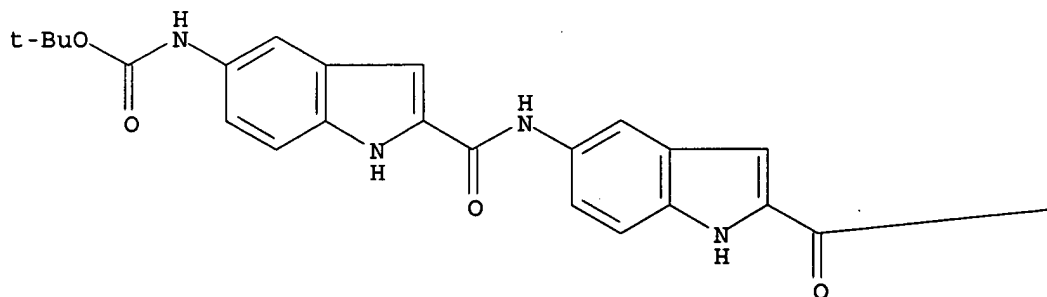
(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

RN 372954-24-0 HCAPLUS

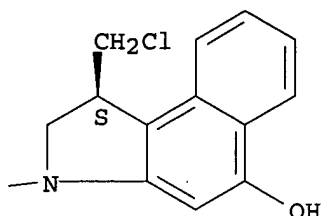
CN Carbamic acid, [2-[[[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L31 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2003:217996 HCAPLUS
 DN 138:238007
 ED Entered STN: 20 Mar 2003
 TI Improved synthesis of (-)-5-hydroxy-1(S)-chloromethyl-1,2-dihydro-3H-benz[e]indole, an intermediate in the preparation of CC-1065 analogs
 IN Yongxin, Robert; Chari, Ravi V. J.
 PA Immunogen, Inc., USA
 SO U.S., 15 pp.
 CODEN: USXXAM
 DT Patent
 LA English
 IC ICM C07D209-56
 NCL 548450000
 CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6534660	B1	20030318	US 2002-116052	20020405 <--
US 6586618	B1	20030701	US 2002-265329	20021007 <--
US 2003195365	A1	20031016	US 2002-265452	20021007 <--
WO 2003087055	A1	20031023	WO 2003-US7276	20030319 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-116052 A3 20020405 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6534660	ICM	C07D209-56
	NCL	548450000
US 2003195365	ECLA	C07D209/60

OS CASREACT 138:238007; MARPAT 138:238007 <--

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Disclosed is an improved synthesis of 5-hydroxy-1(S)-chloromethyl-1,2-

dihydro-3H-benz[e]indole [I; seco(-)CBI] comprising (a) protecting the hydroxy and amino groups of 1-hydroxy-3-naphthylamine with the same protecting group, (b) performing halogenation, alkylation, and ring closure reactions to provide the N,O-protected racemate of I, (c) isolating the (-)-isomer, and (d) removing the protecting groups. By using the same protecting group for the amino and hydroxy groups, this method eliminates redundant protection and deprotection steps, shortens synthesis time, improves product yield, and improves separation of enantiomers. Further disclosed is an improved syntheses of a wide variety of CC-1065 analogs that comprise a CBI alkylating moiety, such as the cell-targeted antitumor antibiotic DC1 and its derivs. For example, 1,3-dihydroxynaphthalene was aminated with NH₃ and converted to N-(tert-butoxycarbonyl)-1-(tert-butoxycarbonyloxy)-3-naphthylamine (69%) with (BOC)₂O in the presence of DIPEA in THF. Iodination with N-iodosuccinimide (86%), alkylation with (Z)-1,3-dichloropropene in the presence of NaH in DMF (93%), and ring closure using Bu₃SnH in the presence of AIBN in benzene (94%) gave the racemic N,O-protected benz[e]indole. The racemic mixture was separated using a chiral HPLC column eluting with 20% i-PrOH in hexane. Deprotection with HCl in the presence of Et₃SiH in EtOAc gave (-)-I•HCl in 90% purity. Two synthetic routes for conversion of (-)-I•HCl to DC1-SMe (II) are also provided.

ST stereoselective secoCBI prepn hydroxynaphthylamine alkylation cyclization; benzindole intermediate CC1065 analog prepn

IT Alkylation
Cyclization

(preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT Protective groups

(tert-butoxycarbonyl; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT 501440-85-3P, 5-(tert-Butoxycarbonyloxy)-3-(tert-butoxycarbonyl)-1-(chloromethyl)-1,2-dihydro-3H-benz[e]indole

RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PYP (Physical process); PREP (Preparation); PROC (Process)

(intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT 501440-87-5P

RL: IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT 16730-20-4P, 5-Nitroindole-2-carboxylic acid 71086-99-2P, Ethyl

5-aminoindole-2-carboxylate 152213-42-8P, tert-Butyl

5-nitroindole-2-carboxylate 152213-43-9P, tert-Butyl

5-aminoindole-2-carboxylate 501440-80-8P 501440-82-0P 501440-84-2P,

2-[N-(tert-Butoxycarbonyl)-N-(3-chloro-2-propen-1-yl)amino]-4-(tert-butoxycarbonyloxy)-1-iodonaphthalene 501440-88-6P, tert-Butyl

5-[[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-carboxylate 501440-90-0P,

tert-Butyl 5-[[[(5-aminoindol-2-yl)carbonyl]amino]indole-2-carboxylate

501440-92-2P 501440-94-4P 501440-95-5P 501440-97-7P 501440-99-9P,

Ethyl 5-[[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-carboxylate

501441-01-6P, 5-[[[(5-Nitroindol-2-yl)carbonyl]amino]indole-2-carboxylic

acid 501441-05-0P, 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole

RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

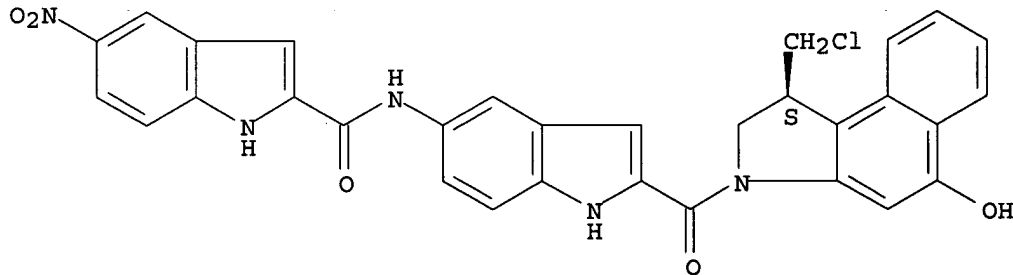
IT 501440-86-4P

RL: BYP (Byproduct); PUR (Purification or recovery); PREP (Preparation)

(preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

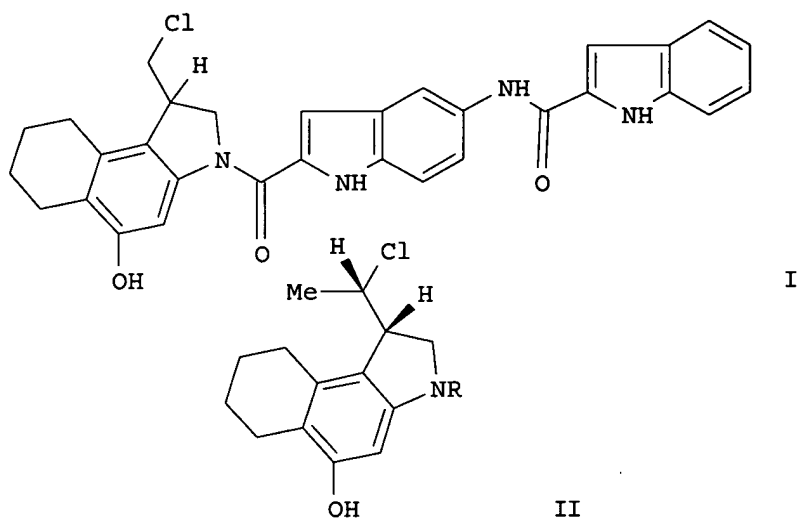
- IT 132-86-5, 1,3-Dihydroxynaphthalene 542-75-6, 1,3-Dichloropropene
16732-57-3, Ethyl 5-nitroindole-2-carboxylate 24424-99-5, Di-tert-butyl
dicarbonate 68617-64-1, 3-(2-Pyridyldithio)propionic acid 138148-59-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of seco(-)CBI as an intermediate in synthesis of CC-1065
analogs)
- IT 130007-89-5P, 5-Hydroxy-1-(S)-((chloromethyl))-1,2-dihydro-3H-
benz[e]indole hydrochloride 299411-68-0P, 5-Hydroxy-1-(S)-
((chloromethyl))-1,2-dihydro-3H-benz[e]indole
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT
(Reactant or reagent)
(target intermediate; preparation of seco(-)CBI as an intermediate in
synthesis of CC-1065 analogs)
- IT 501666-85-9P **501666-87-1P**
RL: IMF (Industrial manufacture); PREP (Preparation)
(target product; preparation of seco(-)CBI as an intermediate in synthesis
of CC-1065 analogs)
- RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
- RE
(1) Boger, D; Chem Rev 1997, V97, P787 HCAPLUS
- IT **501441-05-0P**, 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[[(5-nitroindol-2-
yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT
(Reactant or reagent)
(intermediate; preparation of seco(-)CBI as an intermediate in synthesis of
CC-1065 analogs)
- IT **501666-87-1P**
RL: IMF (Industrial manufacture); PREP (Preparation)
(target product; preparation of seco(-)CBI as an intermediate in synthesis
of CC-1065 analogs)
- IT **501441-05-0P**, 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[[(5-nitroindol-2-
yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT
(Reactant or reagent)
(intermediate; preparation of seco(-)CBI as an intermediate in synthesis of
CC-1065 analogs)
- RN 501441-05-0 HCAPLUS
- CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-
hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-nitro- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



- L31 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
- AN 2002:394360 HCAPLUS
- DN 137:201172
- ED Entered STN: 28 May 2002
- TI Synthesis and biological evaluation of novel analogues and prodrugs of the
cytotoxic antibiotic CC-1065 for selective cancer therapy
- AU Tietze, Lutz F.; Herzig, Tobias; Feuerstein, Tim; Schuberth, Ingrid

CS Georg-August-Universitat Gottingen, Institut fur Organische Chemie,
 Gottingen, 37077, Germany
 SO European Journal of Organic Chemistry (2002), (10), 1634-1645
 CODEN: EJOCFK; ISSN: 1434-193X
 PB Wiley-VCH Verlag GmbH
 DT Journal
 LA English
 CC 26-6 (Biomolecules and Their Synthetic Analogs)
 Section cross-reference(s): 1
 OS CASREACT 137:201172
 GI



AB This paper describes novel seco-analogs, e.g. I, of the cytotoxic antibiotic CC-1065 and their galactoside prodrugs for antibody-directed enzyme prodrug therapy (ADEPT). A partially hydrogenated seco-CCI-analog and the corresponding methyl-CCI analogs were synthesized by alkylation reactions followed by radical cyclization and deprotection. Treatment of the above compds. with the galactose trichloroacetimidate and the bisindolyl-carboxylic acid in the presence of EDC followed by solvolysis gave the desired galactoside prodrugs. In vitro tests showed a strong cytotoxicity for I and a fairly low toxicities for other prepared compds. The selectivity of the galactoside prodrugs was not sufficient for ADEPT. Interestingly, II (R = COOCMe₃) did not undergo Winstein cyclization to produce the spirocyclopropylcyclohexadienone moiety.

ST CC1065 seco analog prepn; alkylation radical cyclization CC1065 analog prepn; antibody directed enzyme prodrug therapy galactoside CC1065

IT Chemotherapy
 (antibody-directed enzyme; synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and antibody-directed enzyme prodrug therapy)

IT Structure-activity relationship
 (antitumor; synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and antibody-directed enzyme prodrug therapy)

IT Bronchi, neoplasm
 (carcinoma; synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and antibody-directed enzyme prodrug therapy)

IT Cyclization
 (radical; synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and

- antibody-directed enzyme prodrug therapy)
- IT Alkylation
Antitumor agents
Human
Neoplasm
(synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and antibody-directed enzyme prodrug therapy)
- IT 452921-65-2P 452921-66-3P 452921-75-4P
452921-76-5P 452921-77-6P 452921-78-7P
452921-79-8P 452921-80-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and antibody-directed enzyme prodrug therapy)
- IT 119-64-2 542-75-6 926-57-8 86520-63-0 101134-91-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and antibody-directed enzyme prodrug therapy)
- IT 50536-99-7P 51522-30-6P 452921-67-4P 452921-68-5P 452921-69-6P
452921-70-9P 452921-71-0P 452921-72-1P 452921-73-2P 452921-74-3P
452921-82-3P 452921-83-4P 452921-84-5P 452921-85-6P 452921-86-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and antibody-directed enzyme prodrug therapy)
- IT 69866-21-3DP, CC 1065, analogs 452921-81-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and antibody-directed enzyme prodrug therapy)
- RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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- IT 452921-65-2P 452921-66-3P 452921-75-4P
452921-76-5P 452921-77-6P 452921-78-7P
452921-79-8P 452921-80-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and antibody-directed enzyme prodrug therapy)

IT 452921-65-2P

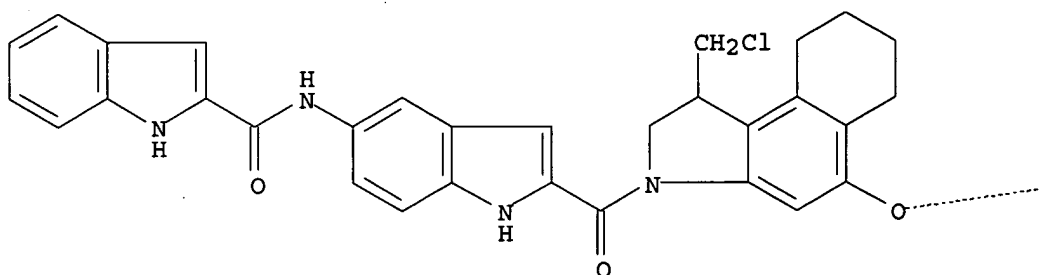
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and biol. evaluation of novel analogs and prodrugs of the cytotoxic antibiotic CC-1065 for selective cancer therapy and antibody-directed enzyme prodrug therapy)

RN 452921-65-2 HCAPLUS

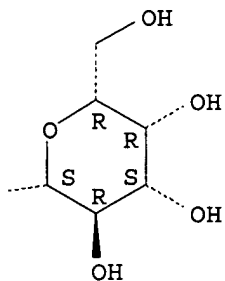
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-5-(β-D-galactopyranosyloxy)-1,2,6,7,8,9-hexahydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L31 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:816635 HCAPLUS

DN 135:344672

ED Entered STN: 09 Nov 2001

TI Preparation of heterocyclic glycosidic prodrugs for use in selective antibody directed enzyme prodrug cancer therapy

IN Tietze, Lutz F.; Fecher, Anja; Herzig, Tobias

PA Germany

SO PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DT Patent

LA German

IC ICM C07D209-00

CC 33-3 (Carbohydrates)

Section cross-reference(s): 1, 27, 63

FAN.CNT 2

PATENT NO.

KIND

DATE

APPLICATION NO.

DATE

trichloroacetimidate, N-deprotection and reaction with 5[[(1H-indol-2'-yl)carbonyl)amino]-1H-indol-2-carboxylic acid, desilylation and chlorination, and sugar O-deacetylation. In in vitro tests with human bronchial carcinoma cell line A549, I showed high activity in the presence of added β -D-galactosidase, but little activity alone, showing that it was an effective prodrug.

ST indole cyclization benzoquinoline galactopyranoside prepn anticancer prodrug cytotoxicity chemotherapy; drug delivery system benzoquinoline galactopyranoside prepn; antibody directed enzyme prodrug therapy benzoquinoline galactopyranoside prepn

IT Chemotherapy
(antibody-directed enzyme; preparation of heterocyclic glycosidic prodrugs for use in selective antibody directed enzyme prodrug cancer therapy)

IT Antitumor agents
Chemotherapy
Cyclization
Cytotoxicity
Drug delivery systems
(preparation of heterocyclic glycosidic prodrugs for use in selective antibody directed enzyme prodrug cancer therapy)

IT Glycosides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heterocyclic glycosidic prodrugs for use in selective antibody directed enzyme prodrug cancer therapy)

IT 330206-90-1P 371155-16-7P 371155-19-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic glycosidic prodrugs for use in selective antibody directed enzyme prodrug cancer therapy)

IT 926-57-8 86520-63-0 101134-91-2 161646-53-3 191732-57-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of heterocyclic glycosidic prodrugs for use in selective antibody directed enzyme prodrug cancer therapy)

IT 330206-88-7P 330206-89-8P 371155-10-1P 371155-11-2P
371155-12-3P 371155-13-4P 371155-14-5P 371155-15-6P 371155-17-8P
371155-18-9P 371155-20-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclic glycosidic prodrugs for use in selective antibody directed enzyme prodrug cancer therapy)

IT 330206-90-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic glycosidic prodrugs for use in selective antibody directed enzyme prodrug cancer therapy)

IT 330206-89-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclic glycosidic prodrugs for use in selective antibody directed enzyme prodrug cancer therapy)

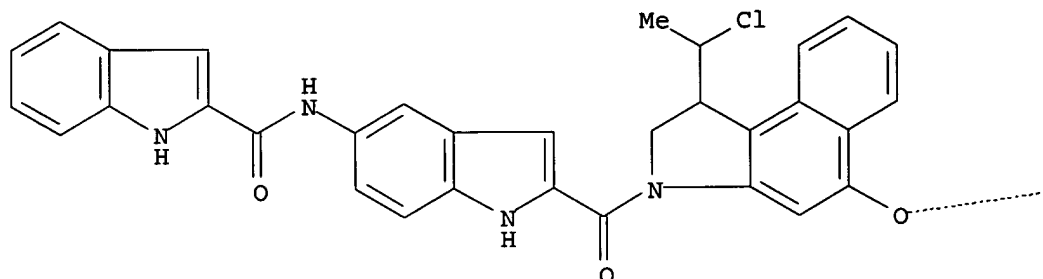
IT 330206-90-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic glycosidic prodrugs for use in selective antibody directed enzyme prodrug cancer therapy)

RN 330206-90-1 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[[1-(1-chloroethyl)-5-(β -D-

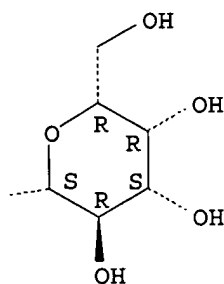
galactopyranosyloxy)-1,2-dihydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L31 ANSWER 6 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2001:752449 HCAPLUS
 DN 136:112208
 ED Entered STN: 16 Oct 2001
 TI Highly selective glycosylated prodrugs of cytostatic CC-1065 analogues for antibody-directed enzyme tumor therapy
 AU Tietze, Lutz F.; Herzig, Tobias; Fecher, Anja; Haunert, Frank; Schuberth, Ingrid
 CS Inst. fur Organische Chemie, Georg-August-Univ., Gottingen, 37077, Germany
 SO ChemBioChem (2001), 2(10), 758-765
 CODEN: CBCHFX; ISSN: 1439-4227
 PB Wiley-VCH Verlag GmbH
 DT Journal
 LA English
 CC 1-3 (Pharmacology)
 OS CASREACT 136:112208
 AB Novel prodrugs of the cytotoxic antibiotic CC-1065 for an antibody-directed enzyme prodrug therapy (ADEPT) were prepared that show an excellent selectivity with a high toxicity of the corresponding drug. In particular, the seco-CBI analog of CC-1065, 1-chloromethyl-5-hydroxy-1,2-dihydro-3H-benz(e)indole, as well as the novel methyl-seco-CBI analog 1-(1'-chloroethyl)-5-hydroxy-1,2-dihydro-3H-benz[e]indole, were synthesized and transformed into their galactosides 10a and 10b, resp. These galactosides can be cleaved with β -D-galactosidase to give the free cytotoxic compds. They were tested in vitro cytotoxicity assays by using human bronchial carcinoma cells of line A549 in the presence and in the absence of β -D-galactosidase. While the seco-CBI prodrugs revealed only modest selectivity, prodrugs of the methyl-seco-CBI analog bearing an anti orientation of the substituents at the two stereogenic centers of the N-heterocycle displayed an excellent selectivity with an

ED50 quotient of about 750. The cytotoxicity of the corresponding phenol was rather high, with an ED50 of 1.3 nM. The diastereomer with a syn orientation at the stereogenic centers was much less toxic.

- ST glycosylated prodrug CC 1065 analog; antibody directed enzyme tumor therapy CC1065 analog
- IT Diastereomers
(CC-1065 analogs; highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)
- IT Chemotherapy
(antibody-directed enzyme; highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)
- IT Cytotoxicity
Human
(highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)
- IT Drug delivery systems
(prodrugs; highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)
- IT 390362-62-6P 390362-63-7P 390362-64-8P
390362-68-2P 390362-69-3P 390362-70-6P
390362-71-7P 390362-72-8P 390362-73-9P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)
- IT 69866-21-3DP, CC-1065, analogs
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)
- IT 542-75-6 926-57-8 25952-53-8, N-Ethyl-N'-(3-dimethylaminopropyl)carbodiimide hydrochloride 86520-63-0 90016-93-6 101134-91-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)
- IT 122745-40-8P 227084-59-5P 330206-87-6P 330206-88-7P 390362-66-0P
390362-67-1P 390362-74-0P 390362-75-1P 697263-39-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)
- IT 122745-41-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)
- IT 9031-11-2, β -Galactosidase
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD

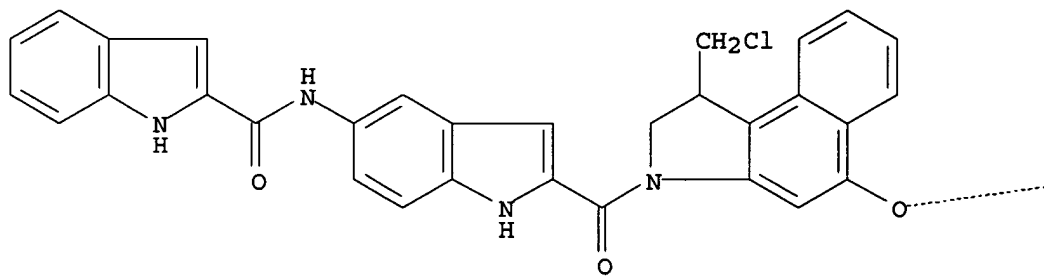
RE

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- (2) Boger, D; Angew Chem 1996, V108, P1542
- (3) Boger, D; Angew Chem Int Ed Engl 1996, V35, P1438 HCAPLUS
- (4) Boger, D; Chem Rev 1997, V97, P787 HCAPLUS
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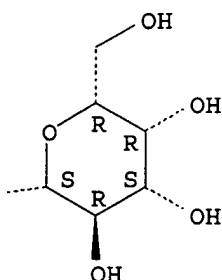
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 (14) Tannock, I; Cancer Res 1989, V49, P4373 MEDLINE
 (15) Tietze, L; Angew Chem 1990, V102, P812 HCAPLUS
 (16) Tietze, L; Angew Chem 1996, V108, P2840
 (17) Tietze, L; Angew Chem Int Ed Engl 1990, V29, P782
 (18) Tietze, L; Angew Chem Int Ed Engl 1996, V35, P2674 HCAPLUS
 (19) Tietze, L; Cancer Res 1989, V49, P4179 HCAPLUS
 (20) Zimmermann, P; J Carbohydr Chem 1988, V7, P435 HCAPLUS
- IT 390362-62-6P 390362-63-7P 390362-64-8P
 390362-68-2P 390362-69-3P 390362-70-6P
 390362-71-7P 390362-72-8P 390362-73-9P
 RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)
- IT 390362-62-6P
 RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (highly selective glycosylated prodrugs of cytostatic CC-1065 analogs for antibody-directed enzyme tumor therapy)
- RN 390362-62-6 HCAPLUS
 CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-5-(β-D-galactopyranosyloxy)-1,2-dihydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



ED Entered STN: 13 Sep 2001

TI Parallel Synthesis and Evaluation of 132 (+)-1,2,9,9a-Tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) Analogues of CC-1065 and the Duocarmycins Defining the Contribution of the DNA-Binding Domain

AU Boger, Dale L.; Schmitt, Harald W.; Fink, Brian E.; Hedrick, Michael P.

CS Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA

SO Journal of Organic Chemistry (2001), 66(20), 6654-6661
CODEN: JOCEAH; ISSN: 0022-3263

PB American Chemical Society

DT Journal

LA English

CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 9

OS CASREACT 135:357786

AB The solution-phase, parallel synthesis and evaluation of a library of 132 (+)-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) analogs of CC-1065 and the duocarmycins containing dimeric monocyclic, bicyclic, and tricyclic heteroarom. replacements for the DNA-binding domain are described. This systematic study revealed clear trends in the structural requirements for observation of potent cytotoxic activity and DNA alkylation efficiency, the range of which spans a magnitude of ≥ 10 000-fold. Combined with related studies, these results highlight that the role of the DNA-binding domain goes beyond simply providing DNA-binding selectivity and affinity (10-100-fold enhancement in properties), consistent with the proposal that it contributes significantly to catalysis of the DNA alkylation reaction accounting for as much as an addnl. 1000-fold enhancement in properties.

ST tetrahydrochloromethylbenzindolone library prepn soln phase; CC1065 duocarmycin analog library cytotoxicity; DNA alkylation binding domain tetrahydrochloromethylbenzindolone library

IT DNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(binding domain; synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

IT Alkylating agents, biological
Combinatorial library
Cytotoxicity
(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

IT 128300-14-1 130007-93-1 135306-53-5 166104-33-2 166104-36-5
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

IT 372953-14-5P 372953-15-6P 372953-16-7P 372953-17-8P 372953-18-9P
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372953-24-7P 372953-25-8P 372953-26-9P 372953-27-0P 372953-28-1P
372953-29-2P 372953-30-5P 372953-31-6P 372953-32-7P 372953-33-8P
372953-34-9P 372953-35-0P 372953-36-1P 372953-37-2P 372953-38-3P
372953-39-4P 372953-40-7P 372953-41-8P 372953-42-9P 372953-43-0P
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372953-65-6P 372953-66-7P 372953-67-8P 372953-68-9P 372953-69-0P
372953-70-3P 372953-71-4P 372953-72-5P 372953-73-6P 372953-74-7P

372953-75-8P	372953-76-9P	372953-77-0P	372953-78-1P	372953-79-2P
372953-80-5P	372953-81-6P	372953-82-7P	372953-83-8P	372953-84-9P
372953-85-0P	372953-86-1P	372953-87-2P	372953-88-3P	372953-89-4P
372953-90-7P	372953-91-8P	372953-92-9P	372953-93-0P	372953-94-1P
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372954-46-6P	372954-47-7P	372954-48-8P		

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

IT 99-05-8, 3-Aminobenzoic acid 150-13-0, 4-Aminobenzoic acid 40283-41-8,
 2-Amino-4-thiazolecarboxylic acid 42933-44-8 45776-13-4 82221-08-7
 89499-38-7 98589-46-9 130007-89-5 152213-40-6 263710-28-7
 372953-12-3 372953-13-4

RL: RCT (Reactant); RACT (Reactant or reagent)
 (synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

RE.CNT 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD
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IT 135306-53-5

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

IT 372954-24-0P

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

IT 135306-53-5

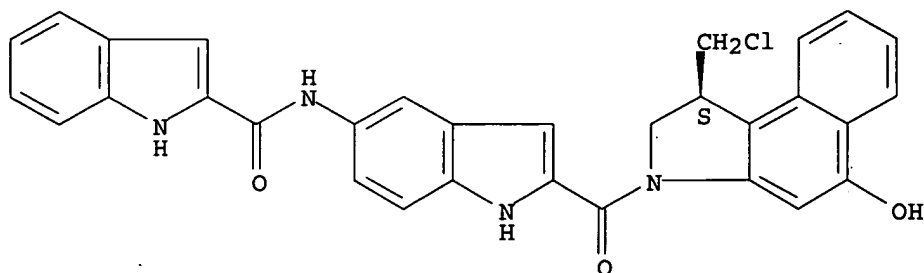
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(synthesis and evaluation of tetrahydrocyclopropa[c]benz[e]indol-4-one analogs of CC-1065 and the duocarmycins defining the contribution of the DNA-binding domain)

RN 135306-53-5 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L31 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:224194 HCAPLUS

DN 134:237751

ED Entered STN: 29 Mar 2001

TI Synthesis of glycosidic prodrugs containing 6-Hydroxy-2,3-dihydro-1H-indolene, 5-Hydroxy-1,2-dihydro-3H-pyrrolo[3,2-e]indolene or 5-Hydroxy-1,2-dihydro-3H-benzo[e]indolene for use in cancer therapy

IN Tietze, Lutz F.; Herzig, Tobias

PA Germany

SO Ger. Offen., 26 pp.

CODEN: GWXXBX

DT Patent

LA German

IC ICM C07H017-08

ICS C07D209-10; C07D487-02; A61K031-40

CC 33-3 (Carbohydrates)

Section cross-reference(s): 1, 27, 63

FAN.CNT 2

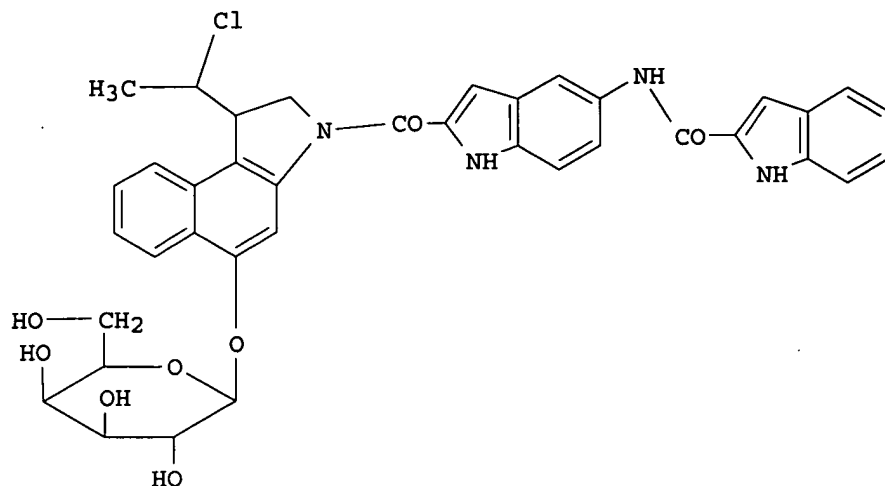
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PI	DE 10021335	A1	20010329	DE 2000-10021335	20000502 <--
	WO 2001083448	A2	20011108	WO 2001-EP4904	20010502 <--
	WO 2001083448	A3	20020620		
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	RW:				
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	R:				
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PRAI	DE 2000-10021335	A	20000502	<--	
	DE 2000-10025329	A	20000523	<--	
	WO 2001-EP4904	W	20010502	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
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	ICS	C07D209-10; C07D487-02; A61K031-40
US 2004033962	ECLA	C07D209/60; C07D487/04; C07H017/02

OS MARPAT 134:237751

GI



AB Title compds. (e.g. I) were prepared as prodrugs for use in the treatment of cancer by the antibody directed enzymic prodrug therapy (ADEPT) method, and were characterized by a high toxicity difference between prodrug and underlying drug and a very high effectiveness of the drug being delivered. Thus, 2-amino-4-benzyloxy-N-((H₃C)₃COC(O))-1-iodonaphthalene was reacted with an E/Z mixture of 1,3-dichlorobut-2-ene, and the product cyclized to give 5-benzyloxy-3-((H₃C)₃COC(O))-1-(1'-chloroethyl)-1,2-dihydro-3H-benzo[e]indole, which was O-deprotected and reacted with o-(2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl)-trichloroacetimidate and 5-[(1H-indol-2'-yl)carbonyl]amino]-1H-indol-2-carboxylic acid to give the tetra-O-acetylated I, which was then O-deprotected to give I. In antiproliferative in vivo tests using cell line A 549 cells, I had ED₅₀ 2 nM, when incubated with β-D-galactosidase vs. ED₅₀ 1470 nM without added enzyme.

ST indolene glycoside cyclization prepn prodrug cancer therapy

IT Antitumor agents

Cyclization

(preparation of glycosidic prodrugs containing substituted indolenes for use in cancer therapy)

IT Glycosides

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of glycosidic prodrugs containing substituted indolenes for use in cancer therapy)

IT Drug delivery systems

(prodrugs; preparation of glycosidic prodrugs containing substituted indolenes for use in cancer therapy)

IT 330206-90-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of glycosidic prodrugs containing substituted indolenes for use in cancer therapy)

IT 7415-31-8 10075-38-4 86520-63-0 101134-91-2 161646-53-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of glycosidic prodrugs containing substituted indolenes for use in cancer therapy)

IT 330206-86-5P 330206-87-6P 330206-88-7P **330206-89-8P**
 330206-91-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation of glycosidic prodrugs containing substituted indolenes for
 use in
 cancer therapy)

IT **330206-90-1P**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of glycosidic prodrugs containing substituted indolenes for
 use in
 cancer therapy)

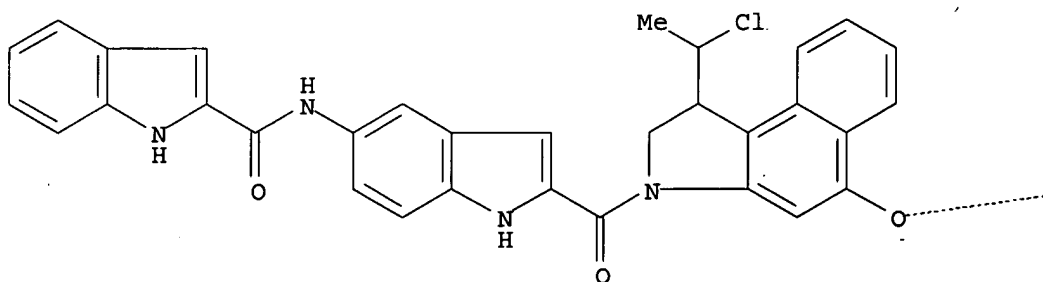
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 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation of glycosidic prodrugs containing substituted indolenes for
 use in
 cancer therapy)

IT **330206-90-1P**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of glycosidic prodrugs containing substituted indolenes for
 use in
 cancer therapy)

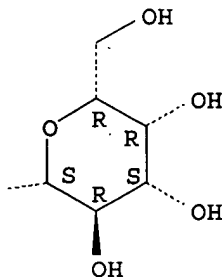
RN 330206-90-1 HCAPLUS
 CN 1H-Indole-2-carboxamide, N-[2-[[1-(1-chloroethyl)-5-(β-D-
 galactopyranosyloxy)-1,2-dihydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-
 yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

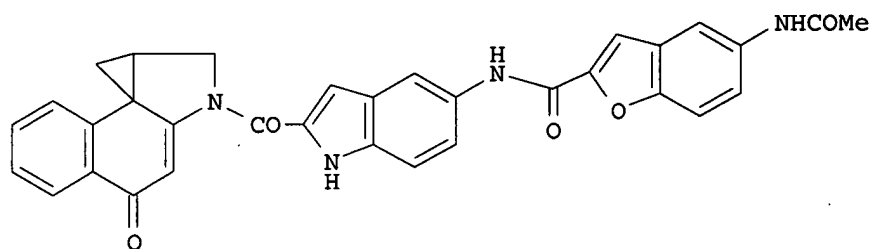
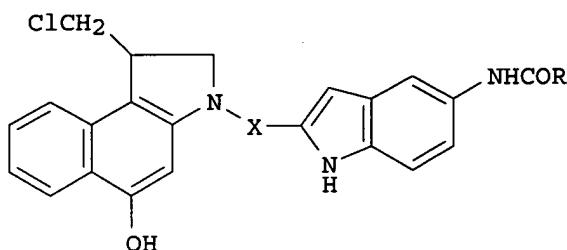
PAGE 1-A



PAGE 1-B



AN 2000:173482 HCAPLUS
 DN 132:321743
 ED Entered STN: 17 Mar 2000
 TI Synthesis and Preliminary Biological Evaluations of CC-1065 Analogues:
 Effects of Different Linkers and Terminal Amides on Biological Activity
 AU Wang, Yuqiang; Yuan, Huiling; Ye, Wenqing; Wright, Susan C.; Wang, Hong;
 Larrick, James W.
 CS Panorama Research Inc., Mountain View, CA, 94043, USA
 SO Journal of Medicinal Chemistry (2000), 43(8), 1541-1549
 CODEN: JMCMAR; ISSN: 0022-2623
 PB American Chemical Society
 DT Journal
 LA English
 CC 26-6 (Biomolecules and Their Synthetic Analogs)
 Section cross-reference(s): 1
 GI



AB CC-1065 analogs possessing a biol. active CBI functional group and amide-substituted indole and benzofuran were synthesized. The IC₅₀ values of compds. (I) (R = 5-acetamino-1H-indol-2-yl; X = CO) (II), bearing two indoles, and I (R = Me; X = CO), bearing only one indole, are 0.4 and 3 nM, resp., against U937 leukemia cells in vitro. The IC₅₀ values of compds. I (R = 5-butyramino-1H-benzofuran-2-yl; X = CO), bearing a butyramino group, and I (R = 5-acetamino-1H-benzofuran-2-yl; X = CO), bearing an acetamino group, are 0.008 and 0.4 nM, resp., against U937 leukemia cells in vitro. I (R = 5-acetamino-1H-indol-2-yl; X = CO-CH=CH), bearing a double-bond linker, is about 4-fold more potent than I (R = Me; X = CO), bearing no double-bond linker. II is highly potent against all cell lines tested in the NCI in vitro screening with IC₅₀ values in the 0.1-5 nM range for most cell lines. II and III are highly active against L1210 leukemia in mice. II is also active against B16BL6 melanoma in mice. Most importantly, II and III are not myelosuppressive at therapeutically EDs. The mechanism of tumor cell death is through induction of apoptosis, and is accompanied by DNA fragmentation.

ST CC 1065 analog prepn; antileukemic activity cytotoxicity CC 1065 analog;
antitumor antibiotic benzofuran indole linker terminal amide effect

IT Antitumor agents
Antitumor agents
(antibiotic; preparation, effects of different linkers and terminal amides
on antitumor activity of CC-1065 analogs)

IT Antibiotics
Antibiotics
(antitumor; preparation, effects of different linkers and terminal amides on
antitumor activity of CC-1065 analogs)

IT Antitumor agents
(leukemia; preparation, effects of different linkers and terminal amides on
antitumor activity of CC-1065 analogs)

IT Cytotoxicity
(of CC-1065 analogs)

IT 69866-21-3P, (+)-CC 1065
RL: PNU (Preparation, unclassified); PREP (Preparation)
(effects of different linkers and terminal amides on biol. activity of
CC-1065 analogs)

IT 199806-51-4P 266349-02-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological
study); PREP (Preparation)
(preparation and antitumor activity of CC-1065 analogs)

IT 199806-32-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological
study); PREP (Preparation)
(preparation and cytotoxicity of CC-1065 analogs)

IT 199806-34-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL
(Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation, DNA fragmentation and cytotoxicity of CC-1065 analogs)

IT 199806-33-2P
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or
effector, except adverse); BSU (Biological study, unclassified); SPN
(Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, cytotoxicity and hematol. effects of CC-1065 analogs)

IT 106-31-0, Butanoic anhydride 2605-67-6 122745-46-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(preparation, effects of different linkers and terminal amides on biol.
activity of CC-1065 analogs)

IT 199806-35-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological
study); PREP (Preparation)
(preparation, effects of different linkers and terminal amides on biol.
activity of CC-1065 analogs)

IT 10242-12-3 16732-57-3 104862-11-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation, effects of different linkers and terminal amides on biol.
activity of CC-1065 analogs)

IT 1646-30-6P 110887-42-8P 199805-80-6P 199805-81-7P 199805-82-8P
199805-89-5P 199805-93-1P 199805-96-4P 199805-99-7P 199806-02-5P
199806-03-6P 199806-04-7P 199806-10-5P 266348-99-6P 266349-00-2P
266349-01-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation, effects of different linkers and terminal amides on biol.
activity of CC-1065 analogs)

RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD

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IT 199806-33-2P

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (preparation, cytotoxicity and hematol. effects of CC-1065 analogs)

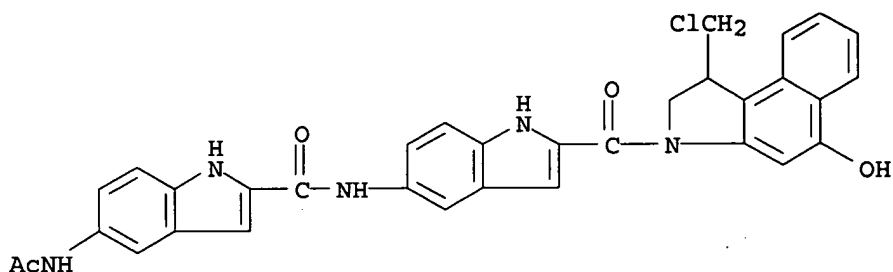
IT 199806-33-2P

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (preparation, cytotoxicity and hematol. effects of CC-1065 analogs)

RN 199806-33-2 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-(acetylamino)-N-[2-[[1-(chloromethyl)-1,2-

dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI)
(CA INDEX NAME)



L31 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1999:550372 HCAPLUS
 DN 131:237670
 ED Entered STN: 31 Aug 1999
 TI CBI prodrug analogs of CC-1065 and the duocarmycins
 AU Boger, Dale L.; Boyce, Christopher W.; Garbaccio, Robert M.; Searcey, Mark; Jin, Qing
 CS Dep. Chemistry, Skaggs Institute Chemical Biology, La Jolla, CA, 92037, USA
 SO Synthesis (1999), (Spec. Iss.), 1505-1509
 CODEN: SYNTBF; ISSN: 0039-7881
 PB Georg Thieme Verlag
 DT Journal
 LA English
 CC 1-6 (Pharmacology)
 Section cross-reference(s): 26
 AB The preparation of a small series of CBI-indole² prodrugs is detailed.
 ST CC1065 CBI prodrug analog antitumor prepn; duocarmycin CBI prodrug analog antitumor prepn
 IT Antitumor agents
 (preparation and antitumor activity of CBI prodrug analogs of CC-1065 and duocarmycins)
 IT Drug delivery systems
 (prodrugs; preparation and antitumor activity of CBI prodrug analogs of CC-1065 and duocarmycins)
 IT 130288-24-3P, Duocarmycin SA 135306-52-4P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); BIOL (Biological study); PREP (Preparation)
 (preparation and antitumor activity of CBI prodrug analogs of CC-1065 and duocarmycins)
 IT 135306-53-5
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
 (preparation and antitumor activity of CBI prodrug analogs of CC-1065 and duocarmycins)
 IT 244154-60-7P 244154-61-8P 244154-62-9P
 244154-63-0P 244154-64-1P 244154-65-2P
 244154-68-5P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation and antitumor activity of CBI prodrug analogs of CC-1065 and duocarmycins)
 IT 69866-21-3P, CC-1065

RL: BSU (Biological study, unclassified); PNU (Preparation, unclassified);
BIOL (Biological study); PREP (Preparation)

(preparation and antitumor activity of CBI prodrug analogs of CC-1065 and
duocarmycins)

IT 103-71-9, Phenyl isocyanate, reactions 109-01-3, N-Methylpiperazine
72547-44-5 101134-91-2 130007-86-2

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation and antitumor activity of CBI prodrug analogs of CC-1065 and
duocarmycins)

IT 244154-66-3P 244154-67-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation and antitumor activity of CBI prodrug analogs of CC-1065 and
duocarmycins)

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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P89
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HCAPLUS
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Interactions 1990, P531 HCAPLUS
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IT 135306-53-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); RCT (Reactant); BIOL (Biological study); RACT
(Reactant or reagent)

(preparation and antitumor activity of CBI prodrug analogs of CC-1065 and
duocarmycins)

IT 244154-60-7P 244154-61-8P 244154-62-9P
244154-63-0P 244154-64-1P 244154-65-2P
244154-68-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological
study); PREP (Preparation)

(preparation and antitumor activity of CBI prodrug analogs of CC-1065 and
duocarmycins)

IT 135306-53-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

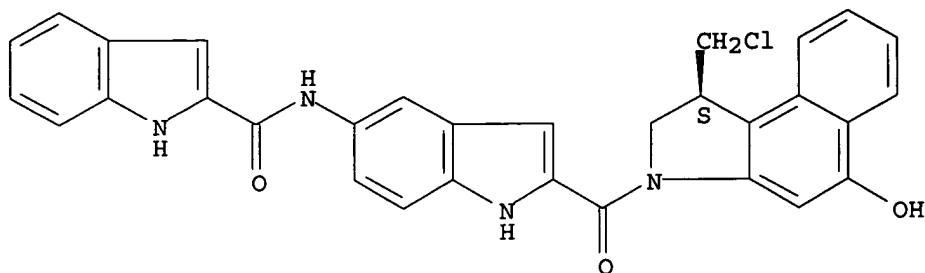
study, unclassified); RCT (Reactant); BIOL (Biological study); RACT
(Reactant or reagent)

(preparation and antitumor activity of CBI prodrug analogs of CC-1065 and
duocarmycins)

RN 135306-53-5 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-
hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX
NAME)

Absolute stereochemistry. Rotation (+).



L31 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:805723 HCAPLUS

DN 128:61379

ED Entered STN: 26 Dec 1997

TI Synthesis and cytotoxic activity of analogs of CC-1065 and the
duocarmycins

IN Boger, Dale L.

PA Scripps Research Institute, USA; Boger, Dale L.

SO PCT Int. Appl., 148 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07D209-90

ICS C07D403-02; C07D403-14; C07D403-06; C07D417-14

CC 26-6 (Biomolecules and Their Synthetic Analogs)

Section cross-reference(s): 1, 63

FAN.CNT 1

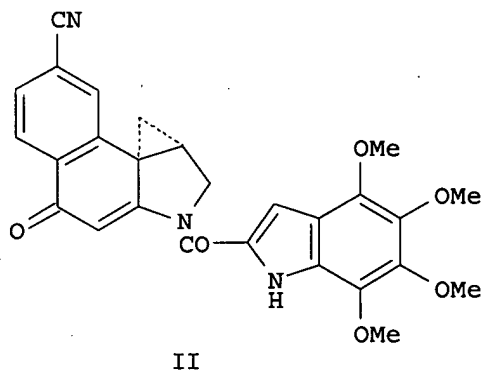
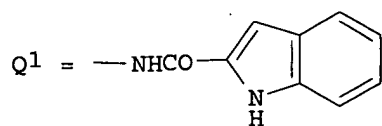
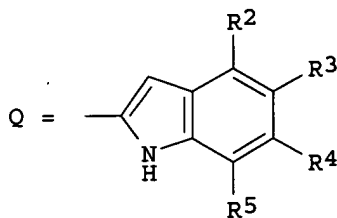
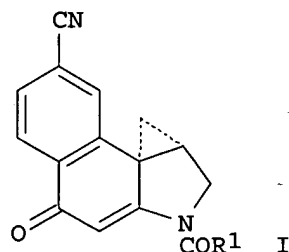
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9745411	A1	19971204	WO 1997-US9076	19970530 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2255703	AA	19971204	CA 1997-2255703	19970530 <--
	AU 9732178	A1	19980105	AU 1997-32178	19970530 <--
	EP 934269	A1	19990811	EP 1997-927807	19970530 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NZ 332960	A	20000526	NZ 1997-332960	19970530 <--
	JP 2000511191	T2	20000829	JP 1997-542909	19970530 <--
	US 6060608	A	20000509	US 1999-194467	19990907 <--
PRAI	US 1996-18860P	P	19960531	<--	
	US 1996-23346P	P	19960912	<--	
	WO 1997-US9076	W	19970530	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9745411	ICM	C07D209-90
	ICS	C07D403-02; C07D403-14; C07D403-06; C07D417-14
US 6060608	ECLA	C07D209/94; C07D209/96; C07D403/06; C07D417/14; C07D487/10

OS MARPAT 128:61379
GI

<--



- AB Analogs of antitumor antibiotics CC-1065 and the duocarmycins I (R1 = C1-C6-alkyl, Q; R2R3 form a pyrrolidine ring containing the vinylene group with the proviso that R4 and R5 = H; R2 = H and R3 = Q1 with the proviso that R4 and R5 = H; R2 = H, R3, R4, R5 = H, MeO) were prepared as compds. which possess systematic and extensive modifications in the DNA binding subunits attached to a 1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) alkylation subunit. The analogs have potent cytotoxic activity and are efficacious antitumor compds. Thus, 3-(tert-butyloxycarbonyl)-1-(chloromethyl)-8-cyano-5-hydroxy-1,2-dihydro-3H-benz[e]indole, prepared in a multistep procedure from m-bromobenzaldehyde and di-Et succinate, was acylated with 5,6,7-trimethoxy-2-indolecarboxylic acid followed by intramol. cyclization to give CCBI-TMI (II). The antitumor IC50(L1210) of II was 7 pM.
- ST antitumor CC1055 duocarmycin analog prepn; cyclopropabenzindolone antitumor antibiotic prepn
- IT Antitumor agents
(synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)
- IT 176442-53-8P 178963-04-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)

IT 178962-98-6P 178962-99-7P 178963-00-3P 178963-01-4P 178963-02-5P
178963-03-6P 181574-83-4P 182957-16-0P 182957-17-1P 182957-18-2P
182957-19-3P 188637-83-4P 188637-86-7P 188637-92-5P 188637-98-1P
188638-21-3P 200352-00-7P 200352-01-8P 200352-02-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)

IT 11116-31-7, Bleomycin A2 69866-21-3, (+)-CC 1065 118292-34-5,
(+)-Duocarmycin A 127379-15-1 128300-13-0 130007-87-3 130288-24-3,
(+)-Duocarmycin SA 132746-32-8 144732-53-6 155861-66-8 155861-67-9
155861-68-0 155861-69-1 155861-70-4 157035-51-3 157035-51-3
188638-16-6 188638-17-7 200351-88-8 200351-92-4 200351-94-6
200351-97-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)

IT 178877-12-8P 178877-13-9P 178877-14-0P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)

IT 106-95-6, Allyl bromide, reactions 123-25-1, Diethyl succinate
870-63-3 1477-50-5, 1H-Indole-2-carboxylic acid 3132-99-8,
3-Bromobenzaldehyde 4382-54-1 4755-77-5 14794-31-1 15026-17-2
16732-73-3 24610-33-1 62209-77-2 77924-28-8 78175-36-7
82692-00-0 101134-91-2 105518-47-6 122745-36-2 128781-07-7
130007-86-2

RL: RCT (Reactant); RACT (Reactant or reagent)

(synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)

IT 130007-89-5P 178876-98-7P 178877-00-4P 178877-02-6P 178877-03-7P
178877-04-8P 178877-05-9P 178877-06-0P 178877-07-1P 178877-08-2P
178877-09-3P 178877-11-7P 178877-17-3P 178877-18-4P 178877-19-5P
178877-31-1P 178877-32-2P 178877-33-3P 178877-34-4P
181574-69-6P 181574-70-9P 181574-71-0P 181574-72-1P 181574-73-2P
181574-74-3P 181574-75-4P 181574-76-5P 181574-77-6P 181574-78-7P
181574-79-8P 181574-80-1P 181574-81-2P 181574-82-3P 181574-85-6P
182957-20-6P 182957-21-7P 182957-22-8P 182957-23-9P 182957-24-0P
188638-12-2P 188638-13-3P 188638-14-4P 188638-15-5P 188638-20-2P
200351-76-4P 200351-81-1P 200351-85-5P 200351-86-6P 200351-91-3P
200351-98-0P 200352-03-0P 200352-04-1P 200352-05-2P 200352-06-3P
200352-07-4P 200352-08-5P 200352-09-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)

IT 178876-99-8P 178877-27-5P 178877-28-6P 178877-29-7P 178877-30-0P
178962-97-5P 178963-05-8P 181574-86-7P 181574-88-9P 181574-89-0P
188638-07-5P 188638-11-1P 188638-19-9P 200351-75-3P 200351-87-7P
200351-89-9P 200351-90-2P 200351-99-1P 200352-10-9P

RL: SPN (Synthetic preparation); PREP (Preparation)

(synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)

IT 178877-33-3P 178877-34-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and cytotoxic activity of analogs of CC-1065 and the

duocarmycins)

IT 178877-33-3P

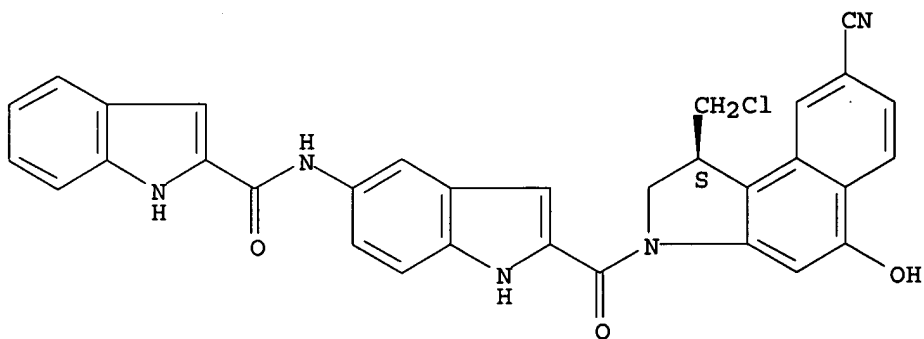
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)

RN 178877-33-3 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-8-cyano-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L31 ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:783786 HCAPLUS

DN 128:48468

ED Entered STN: 15 Dec 1997

TI Preparation of DNA-binding glucuronide indoles immuno-conjugates as antitumors

IN Wang, Yuqiang; Wright, Susan C.; Larrick, James W.

PA Panorama Research, Inc., USA

SO PCT Int. Appl., 79 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K

CC 33-8 (Carbohydrates)

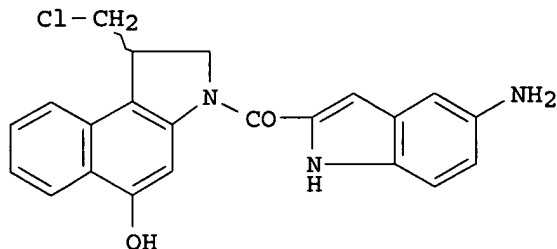
Section cross-reference(s): 1, 34, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9744000	A2	19971127	WO 1997-US9055	19970522 <--
	WO 9744000	A3	19971231		
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	US 5843937	A	19981201	US 1996-652883	19960523 <--
	AU 9732170	A1	19971209	AU 1997-32170	19970522 <--
	EP 918752	A2	19990602	EP 1997-927798	19970522 <--
	R:	AT, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE			
	CN 1219841	A	19990616	CN 1997-194862	19970522 <--
	JP 2000511893	T2	20000912	JP 1997-542898	19970522 <--
PRAI	US 1996-652883	A	19960523		<--

WO 1997-US9055 W 19970522 <--
 CLASS
 PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES

 WO 9744000 ICM A61K
 US 5843937 ECLA C07D403/06; C07D403/06; C07D403/14; C07D405/14;
 C07D495/04; C07D501/00; C07H015/24 <--
 OS MARPAT 128:48468
 GI



AB The present invention relates to novel DNA alkylating agents and the prodrugs of these agents which are useful as antitumors and DNA labeling agents. The compds. are hydroxydihydrobenzindole oligopeptides and prodrugs thereof wherein the monomeric constituents are derived from monocyclic, or bicyclic heterocyclic aromatic residues. Thus, indole I was prepared and tested for its antitumor activity with cytotoxicity (IC50 = 0.09 nM).

ST alkylating agent DNA glucuronide indole prepn; oligopeptide indole prepn antitumor cytotoxicity; DNA labeling agent glucuronide indole prepn; glucuronide indole prepn antitumor

IT Alkylation
 (agents, DNA; preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

IT Glycosides
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (glucuronides, hydroxydihydrobenzindole; preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

IT Peptides, preparation
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (oligopeptides, hydroxydihydrobenzindole; preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

IT Antitumor agents
 Cytotoxicity
 (preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

IT DNA
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

IT 636-47-5P, Distamycin 3 1438-30-8P, Netropsin 38099-64-8P
 110314-48-2P, Adozelesin 112243-81-9P 115308-98-0P, FCE 24517
 122745-33-9P 134106-78-8P 149207-46-5P 199806-22-9P 199806-30-9P
 199806-31-0P 199806-32-1P 199806-33-2P 199806-34-3P
 199806-35-4P 199806-36-5P 199806-37-6P 199806-38-7P

199806-39-8P 199806-40-1P 199806-41-2P
 199806-42-3P 199806-43-4P 199806-44-5P 199806-45-6P
 199806-46-7P 199806-47-8P 199806-48-9P 199806-49-0P 199806-50-3P
 199806-51-4P 199806-52-5P 199806-53-6P 199806-54-7P 199806-55-8P
 199806-56-9P 199806-57-0P 199806-59-2P 199806-60-5P

199806-61-6P 199806-62-7DP, monoclonal antibody
 conjugate 199806-63-8P 199806-64-9P 199806-65-0P
 199986-15-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

IT 496-41-3, 2-Benzofurancarboxylic acid 16732-57-3 21085-72-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

IT 1646-29-3P 1646-30-6P 71086-99-2P 110887-42-8P 138730-80-0P
 138730-81-1P 199805-80-6P 199805-81-7P 199805-82-8P 199805-89-5P
 199805-93-1P 199805-96-4P 199805-99-7P 199806-02-5P 199806-03-6P
 199806-04-7P 199806-07-0P 199806-10-5P 199806-14-9P 199806-15-0P
 199806-16-1P 199806-17-2P 199806-18-3P 199806-19-4P 199806-20-7P
 199806-21-8P 199806-23-0P 199806-24-1P 199806-25-2P 199806-26-3P
 199806-27-4P 199806-28-5P 199806-29-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

IT 199806-33-2P 199806-38-7P 199806-39-8P
 199806-41-2P 199806-42-3P 199806-61-6P
 199806-62-7DP, monoclonal antibody conjugate 199806-64-9P
 199806-65-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

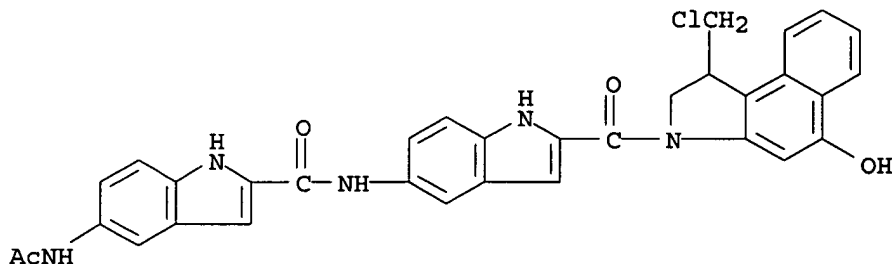
IT 199806-33-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

RN 199806-33-2 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-(acetlamino)-N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI)
 (CA INDEX NAME)



AN 1997:618073 HCAPLUS
 DN 127:262561
 ED Entered STN: 27 Sep 1997
 TI synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the
 duocarmycins
 IN Boger, Dale L.
 PA Scripps Research Institute, USA; Boger, Dale L.
 SO PCT Int. Appl., 92 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM C07D209-70
 ICS C07D403-06; C07D403-14; A61K031-40
 CC 26-6 (Biomolecules and Their Synthetic Analogs)
 Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9732850	A1	19970912	WO 1997-US3641	19970307 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2246783	AA	19970912	CA 1997-2246783	19970307 <--
	AU 9719902	A1	19970922	AU 1997-19902	19970307 <--
	AU 711974	B2	19991028		
	EP 888301	A1	19990107	EP 1997-908059	19970307 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2000506168	T2	20000523	JP 1997-531987	19970307 <--
	US 5985908	A	19991116	US 1998-142337	19980904 <--
PRAI	US 1996-13024P	P	19960308	<--	
	WO 1997-US3641	W	19970307	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9732850	ICM	C07D209-70
	ICS	C07D403-06; C07D403-14; A61K031-40

OS MARPAT 127:262561
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB MCBI (7-methoxy-1,2,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one) (I) (R1 = H) is employable as a DNA alkylating agent and can be incorporated into analogs of CC-1065 and the duocarmycins I (R1 = Q1, Q2, Q3, Q4) for constructing regioselective DNA alkylating agents. Thus, I (R1 = Q1) (II) is prepared by reacting 1-(chloromethyl)-5-hydroxy-8-methoxy-1,2-dihydro-3H-benz[e]indole with Q1-CO2H followed by cyclopropanation with NaH in THF-DMF. The relative rates of DNA alkylation do not follow the relative rates of acid-catalyzed solvolysis.

ST cyclopropabenzindolone DNA alkylating agent prepn; MCBI CC 1065 duocarmycin analog prepn

IT Antitumor agents
 (antibiotic; synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)

IT Antibiotics
(antitumor; synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)

IT Alkylating agents, biological
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)

IT DNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)

IT 173655-21-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)

IT 173655-22-6P 173655-25-9P 173655-26-0P 173655-27-1P 173655-28-2P
173655-29-3P 173655-30-6P 173655-31-7P 173655-32-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)

IT 173655-23-7P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)

IT 173483-64-2P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)

IT 106-95-6, Allyl bromide, reactions 123-25-1, Diethyl succinate
591-31-1, 3-Methoxybenzaldehyde 870-63-3 2564-83-2 62209-77-2
77924-28-8 101134-91-2 105518-47-6 107474-59-9 128781-07-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)

IT 151502-65-7P 157188-04-0P 173483-53-9P 173483-54-0P 173483-55-1P
173483-61-9P 173483-62-0P 173483-63-1P 173483-65-3P 173483-66-4P
173483-74-4P **173483-78-8P** 173483-82-4P 173483-86-8P
196306-01-1P 196306-02-2P 196306-03-3P 196306-04-4P 196306-10-2P
196306-21-5P 196306-22-6P 196306-23-7P 196306-25-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)

IT 92191-07-6P 196306-24-8P 196306-26-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)

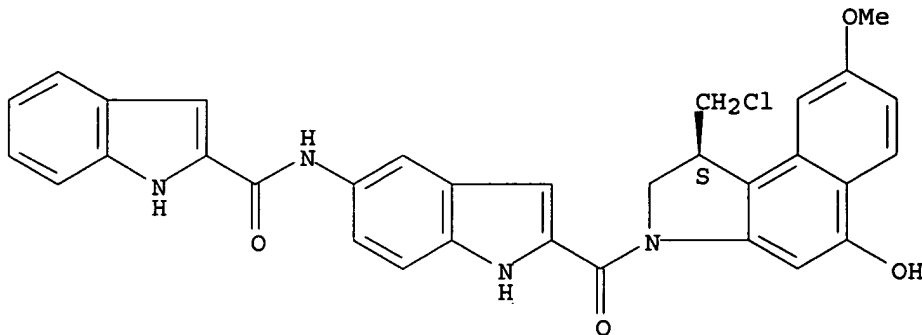
IT **173483-78-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)

IT **173483-78-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)

RN 173483-78-8 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-8-methoxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L31 ANSWER 14 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1997:366275 HCAPLUS
 DN 126:330520
 ED Entered STN: 12 Jun 1997
 TI Preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents
 IN Boger, Dale L.
 PA Scripps Research Institute, USA; Boger, Dale L.
 SO PCT Int. Appl., 140 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM C07D209-90
 ICS C07D403-02; C07D403-14; C07D413-06; C07D417-06
 CC 26-6 (Biomolecules and Their Synthetic Analogs)
 Section cross-reference(s): 1

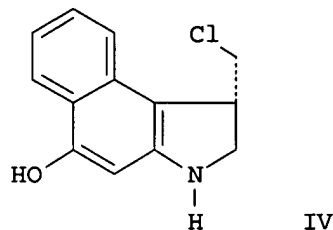
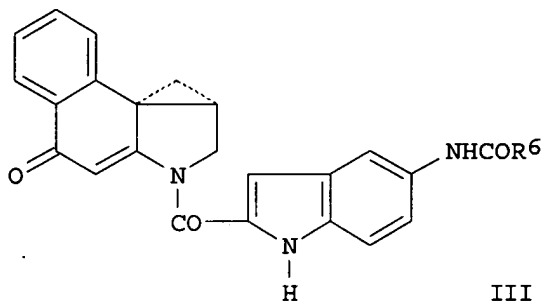
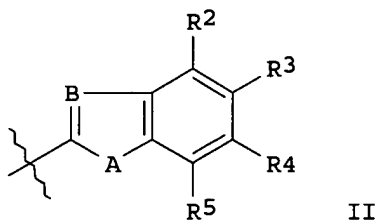
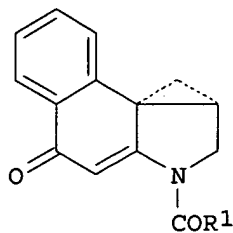
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9712862	A1	19970410	WO 1996-US16481	19961003 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG				
CA 2233936	AA	19970410	CA 1996-2233936	19961003 <--
AU 9674315	A1	19970428	AU 1996-74315	19961003 <--
AU 727608	B2	20001214		
EP 862553	A1	19980909	EP 1996-936498	19961003 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
JP 11513391	T2	19991116	JP 1996-514522	19961003 <--
NZ 321172	A	20000228	NZ 1996-321172	19961003 <--
US 6548530	B1	20030415	US 1998-51264	19981002 <--
US 2004002528	A1	20040101	US 2003-417043	20030415 <--
PRAI US 1995-4752P	P	19951003	<--	
WO 1996-US16481	W	19961003	<--	
US 1998-51264	A1	19981002	<--	

CLASS

PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES

 WO 9712862 ICM C07D209-90
 ICS C07D403-02; C07D403-14; C07D413-06; C07D417-06
 US 2004002528 ECLA C07C281/02; C07D209/42; C07D209/60; C07D209/96;
 C07D307/85; C07D335/06A; C07D405/12; C07D405/14;
 C07D405/14; C07D409/12; C07D409/12; C07D009/14;
 C07D409/14; C07D487/04; C07D498/04; C07D <--
 GI



AB Analogs I [R1 = alkyl, amino, alkyloxy, hydrazinyl, radical (II); A = NH, O; B = C, N; R2R3 = vinylene group; R2-R3 = H, OH, alkyl, alkyloxy, pyrrolidinyl; R4-R5 = H, OH, alkyl, alkyloxy] of the antibiotics CC-1065 and the duocarmycins, containing the 1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) alkylation subunit, where prepared and shown to have potent cytotoxic activity and use as antitumor agents. Thus, amide III (R6 = 2-indolyl) was prepared starting from Me 5-nitro-2-indolecarboxylate, 2-indolecarboxylic acid and aromatic alc. IV and had an IC50 value of 10 pM when tested against L1210 cells. A direct relationship between functional stability and in vitro cytotoxic potency was shown. The CBI-based analogs were easily synthesized and were 4X more stable and 4X more potent than the corresponding analogs containing the authentic CPI alkylation subunit of CC-1065 and comparable in potency to agents containing the authentic alkylation subunit of duocarmycin SA. Similarly, the CBI-based agents alkylate DNA with an unaltered sequence selectivity at an enhanced rate and with a greater efficiency than the corresponding CPI analog and were comparable to the corresponding analog incorporating the duocarmycin SA alkylation subunit. Systematic and extensive modifications and simplifications in the DNA binding subunits attached to CBI were also described.

ST cyclopropabenzindolone duocarmycin analog prepn antitumor; duocarmycin analog prepn antitumor agent; CC1065 analog prepn antitumor agent; DNA alkylating agent duocarmycin analog prepn

IT Antitumor agents
 (preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

IT DNA
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)

(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

IT 128300-13-0P 128571-50-6P 130007-87-3P 130007-90-8P 155861-68-0P
166104-31-0P 166104-34-3P 172375-74-5P 172375-77-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

IT 135306-52-4P 141781-45-5P 155861-67-9P 155861-69-1P 155861-70-4P
166104-32-1P 166104-33-2P 166104-35-4P 166104-36-5P 166372-37-8P
167027-31-8P 167027-38-5P 167027-39-6P 167027-40-9P 172375-79-0P
172375-80-3P 172375-81-4P 172375-82-5P 172375-83-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

IT 69866-21-3, (+)-CC 1065 101222-80-4, (+)-U 71184 104713-39-5
110352-06-2 110352-07-3, (-)-CC 1065 114251-19-3 114977-72-9
118292-34-5, (+)-Duocarmycin A 127232-82-0 127306-33-6 127379-15-1
128300-14-1 128300-15-2 128300-16-3 128300-17-4 130288-24-3,
(+)-Duocarmycin SA 132746-32-8 144732-53-6 149195-48-2
149405-55-0, (-)-Duocarmycin A 151062-84-9, (-)-Duocarmycin SA
157035-50-2 157035-51-3 157922-78-6 157968-94-0 166372-38-9
172491-26-8 172491-27-9 172491-29-1 172491-30-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

IT 79-03-8, Propionyl chloride 99-61-6, 3-Nitrobenzaldehyde 106-95-6,
Allyl bromide, reactions 496-41-3, 2-Benzofurancarboxylic acid
555-16-8, 4-Nitrobenzaldehyde, reactions 624-83-9, Methyl isocyanate
870-46-2, tert-Butylcarbazate 1477-50-5, 1H-Indole-2-carboxylic acid
1816-92-8, Methyl 2-azidoacetate 1953-54-4, 5-Hydroxyindole 2564-83-2,
Tempo 6146-52-7, 5-Nitroindole 6314-28-9, Benzo[b]thiophene-2-
carboxylic acid 7497-12-3 10242-12-3, 5-Nitrobenzofuran-2-carboxylic
acid 19810-31-2, Benzyloxyacetyl chloride 38336-04-8,
2-Benzyloxyethylamine 104862-11-5, Methyl 5-Nitrobenzofuran-2-
carboxylate 120506-51-6 122745-36-2

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

IT 1646-29-3P 64512-81-8P 101134-91-2P 110314-42-6P 122745-39-5P
128300-11-8P 136818-66-1P 147539-80-8P 154272-33-0P 154272-34-1P
154272-35-2P 154294-77-6P 157649-56-4P 161646-53-3P 161646-54-4P
161646-55-5P 166104-12-7P 166104-13-8P, 6H-Pyrrolo[3,2-e]benzoxazole-2-
methanol 166104-14-9P 166104-15-0P 166104-16-1P 166104-18-3P
166104-19-4P 166104-20-7P 166104-21-8P 166104-22-9P 166104-23-0P
166104-24-1P 166104-25-2P 166104-26-3P 166104-27-4P 166104-28-5P
166104-37-6P 167027-28-3P 167027-29-4P 167027-30-7P 167027-32-9P
167027-33-0P 167027-34-1P 172375-67-6P 172375-68-7P 172375-69-8P
172375-70-1P 172375-71-2P 172375-72-3P 172375-85-8P 189124-88-7P
189124-89-8P 189124-90-1P 189124-91-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

IT 130007-86-2P 130007-89-5P 135306-53-5P 172375-61-0P
172375-62-1P 172375-63-2P 172375-64-3P 172375-65-4P 172375-66-5P

172375-73-4P 172375-75-6P 172375-76-7P 172375-78-9P
 172375-86-9P 172491-23-5P 189124-84-3P 189124-85-4P

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
 USES (Uses)

(preparation of analogs of CC-1065 and the duocarmycins, containing the
 cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

IT 166104-17-2P 172375-88-1P 172491-21-3P 172491-22-4P 172491-25-7P
 189124-86-5P 189124-87-6P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); USES (Uses)

(preparation of analogs of CC-1065 and the duocarmycins, containing the
 cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

IT 135306-53-5P 172375-73-4P

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
 USES (Uses)

(preparation of analogs of CC-1065 and the duocarmycins, containing the
 cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

IT 135306-53-5P

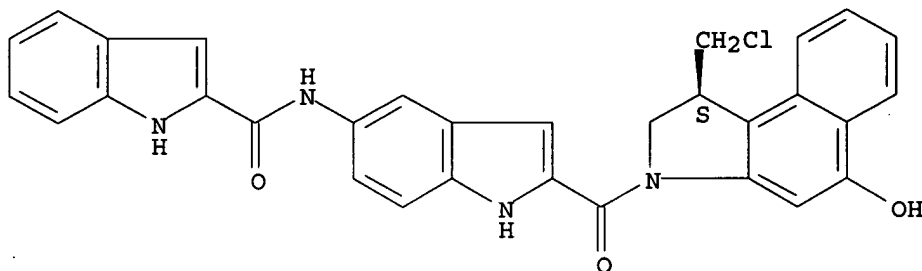
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
 USES (Uses)

(preparation of analogs of CC-1065 and the duocarmycins, containing the
 cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

RN 135306-53-5 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-
 hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry. Rotation (+).



L31 ANSWER 15 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1996:401674 HCAPLUS

DN 125:114357

ED Entered STN: 12 Jul 1996

TI Synthesis, Chemical Properties, and Preliminary Evaluation of Substituted
 CBI Analogs of CC-1065 and the Duocarmycins Incorporating the
 7-Cyano-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one Alkylation
 Subunit: Hammett Quantitation of the Magnitude of Electronic Effects on
 Functional Reactivity

AU Boger, Dale L.; Han, Nianhe; Tarby, Christine M.; Boyce, Christopher W.;
 Cai, Hui; Jin, Qing; Kitos, Paul A.

CS Department of Chemistry, Scripps Research Institute, La Jolla, CA, 92037,
 USA

SO Journal of Organic Chemistry (1996), 61(15), 4894-4912

CODEN: JOCEAH; ISSN: 0022-3263

PB American Chemical Society

DT Journal

LA English

CC 26-6 (Biomolecules and Their Synthetic Analogs)

AB The synthesis of 7-cyano-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (CCBI), a substituted CBI derivative bearing a C(7) cyano group, is described in efforts that establish the magnitude of potential electronic effects on the functional reactivity of the agents. The CCBI alkylation subunit was prepared by a modified Stobbe condensation/Friedel-Crafts acylation for generation of the appropriately functionalized naphthalene precursors followed by 5-exo-trig aryl radical-alkene cyclization for synthesis of the 1,2-dihydro-3H-benz[e]indole skeleton and final Ar-3' alkylation for introduction of the activated cyclopropane. The most concise approach provided the CCBI subunit and its immediate precursor in 14-15 steps in superb overall conversions (15-20%). Resolution of an immediate CCBI precursor and its incorporation into both enantiomers of analogs of CC-1065 and the duocarmycins, are detailed. A study of the solvolysis reactivity and regioselectivity of N-BOC-CCBI revealed that introduction of the C(7) nitrile slowed the rate of solvolysis but only to a surprisingly small extent. Classical Hammett quantitation of the effect provided a remarkably small ρ (-0.3), indicating an exceptionally small C(7) substituent electronic effect on functional reactivity. Addnl. kinetic studies of acid-catalyzed nucleophilic addition proved inconsistent with C(4) carbonyl protonation as the slow and rate-determining step but consistent with a mechanism in which protonation is rapid and reversible followed by slow and rate-determining nucleophilic addition to the cyclopropane requiring both the presence and assistance of a nucleophile (SN2 mechanism). No doubt this contributes to the DNA alkylation selectivity of this class of agents and suggests that the positioning of an accessible nucleophile (adenine N-3) and not C(4) carbonyl protonation is the rate-determining step controlling the sequence selectivity of the DNA alkylation

reaction. This small electronic effect on the solvolysis rate had no impact on the solvolysis regioselectivity, and stereoelectronically-controlled nucleophilic addition to the least substituted carbon of the activated cyclopropane was observed exclusively. Consistent with past studies, a direct relationship between solvolysis stability and cytotoxic potency was observed with the CCBI-derived agents providing the most potent analogs in the CBI series, and these observations were related to the predictable Hammett substituent effects. For the natural enantiomers, this unusually small electronic effect on functional reactivity had no perceptible effect on their DNA alkylation selectivity. Similar effects of the C(7) cyano substituent on the unnatural enantiomers were observed, and they proved to be 4-10 times more effective than the corresponding CBI-based unnatural enantiomers and 4-70 times less potent than the CCBI natural enantiomers.

ST cyanotetrahydrocyclopropabenzindole analog CC1065 duocarmycin prepn
solvolysis; DNA alkylation cyanotetrahydrocyclopropabenzindole analog
CC1065 duocarmycin

IT Inductive effect

(Hammett quantitation of the electronic effects on functional reactivity of cyanotetrahydrocyclopropabenzindole analogs of CC1065 and duocarmycins)

IT Deoxyribonucleic acids

RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(alkylation of DNA by cyanotetrahydrocyclopropabenzindole analogs of CC1065 and duocarmycins)

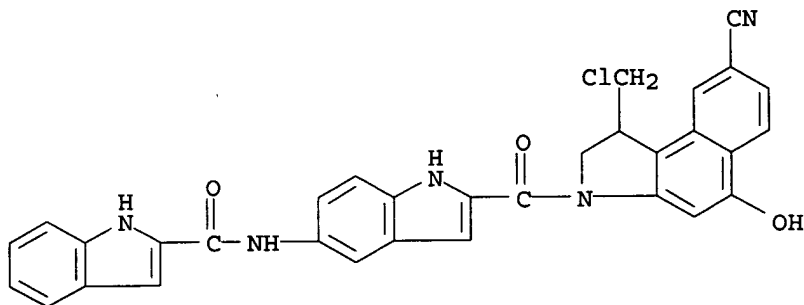
IT Solvolysis

(preparation and solvolysis of cyanotetrahydrocyclopropabenzindole analogs of CC1065 and duocarmycins)

IT 69866-21-3DP, (+)-CC-1065, analogs 118292-34-5DP, (+)-Duocarmycin A, analogs 130288-24-3DP, (+)-Duocarmycin SA, analogs

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

- (preparation and solvolysis of cyanotetrahydrocyclopropabenzindole analogs of CC1065 and duocarmycins)
- IT 178877-21-9P 178877-23-1P 178877-25-3P 178962-98-6P 178962-99-7P
178963-00-3P 178963-01-4P 178963-02-5P 178963-03-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
- (preparation and solvolysis of cyanotetrahydrocyclopropabenzindole analogs of CC1065 and duocarmycins)
- IT 123-25-1, Diethyl succinate 3132-99-8, 3-Bromobenzaldehyde 62209-77-2
77924-28-8 101134-91-2 105518-47-6 128781-07-7
RL: RCT (Reactant); RACT (Reactant or reagent)
- (preparation and solvolysis of cyanotetrahydrocyclopropabenzindole analogs of CC1065 and duocarmycins)
- IT 176442-53-8P 178876-98-7P 178876-99-8P 178877-00-4P 178877-01-5P
178877-02-6P 178877-03-7P 178877-04-8P 178877-05-9P 178877-06-0P
178877-07-1P 178877-08-2P 178877-09-3P 178877-10-6P 178877-11-7P
178877-12-8P 178877-13-9P 178877-14-0P 178877-15-1P 178877-17-3P
178877-18-4P 178877-19-5P 178877-20-8P **178877-22-0P**
178877-24-2P 178877-27-5P 178877-28-6P 178877-29-7P 178877-30-0P
178877-31-1P 178877-32-2P **178877-33-3P 178877-34-4P**
178877-35-5P 178877-36-6P 178877-37-7P 178962-96-4P 178962-97-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
- (preparation and solvolysis of cyanotetrahydrocyclopropabenzindole analogs of CC1065 and duocarmycins)
- IT 178877-16-2P 178877-26-4P 178963-04-7P 178963-05-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
- (preparation and solvolysis of cyanotetrahydrocyclopropabenzindole analogs of CC1065 and duocarmycins)
- IT 128300-13-0 173655-21-5
RL: RCT (Reactant); RACT (Reactant or reagent)
- (solvolysis of)
- IT **178877-22-0P 178877-33-3P 178877-34-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
- (preparation and solvolysis of cyanotetrahydrocyclopropabenzindole analogs of CC1065 and duocarmycins)
- IT **178877-22-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
- (preparation and solvolysis of cyanotetrahydrocyclopropabenzindole analogs of CC1065 and duocarmycins)
- RN 178877-22-0 HCAPLUS
- CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-8-cyano-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



L31 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:113769 HCAPLUS
DN 124:175648
ED Entered STN: 23 Feb 1996
TI Synthesis and Properties of Substituted CBI Analogs of CC-1065 and the
Duocarmycins Incorporating the 7-Methoxy-1,2,9,9a-
tetrahydrocyclopropa[c]benz[e]indol-4-one (MCBI) Alkylation Subunit:
Magnitude of Electronic Effects on the Functional Reactivity
AU Boger, Dale L.; McKie, Jeffrey A.; Cai, Hui; Cacciari, Barbara; Baraldi,
P. G.
CS Department of Chemistry, Scripps Research Institute, La Jolla, CA, 92037,
USA
SO Journal of Organic Chemistry (1996), 61(5), 1710-29
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1
AB The synthesis of 7-methoxy-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-
one (MCBI), a substituted CBI derivative bearing a methoxy group para to the
carbonyl, is described in efforts that establish the magnitude of
potential electronic effects on the chemical and functional reactivity of the
agents. The core structure of the MCBI alkylation subunit was prepared by a
modified Stobbe condensation/Friedel-Crafts acylation for generation of
the appropriately functionalized naphthalene precursors followed by
5-exo-trig aryl radical-alkene cyclization for completion of the synthesis
of the 1,2-dihydro-3H-benz[e]indole skeleton and final Ar-3' alkylation
for introduction of the activated cyclopropane. Two approaches to the
implementation of the key 5-exo-trig free radical cyclization are detailed
with the former proceeding with closure to provide the naphthindole in
which the required product functionalization was introduced prior to
cyclization and the latter with Tempo trap of the cyclization product of
the unfunctionalized alkene substrate. The latter concise approach
provided the MCBI subunit and its immediate precursor in 12-13 steps in
superb overall conversions (27-30%). Resolution of an immediate MCBI
precursor and its incorporation into both enantiomers of analogs of
CC-1065 and the duocarmycins, are detailed. A study of the solvolysis
reactivity and regioselectivity of N-BOC-MCBI revealed that introduction
of the C-7 methoxy group accelerates the rate of solvolysis by only
1.2-1.06 times. This remarkably modest effect is inconsistent with C4
carbonyl protonation as the slow and rate-determining step of solvolysis or
acid-catalyzed nucleophilic addition but is consistent with a mechanism in
which protonation is rapid and reversible followed by slow and rate-determining
nucleophilic addition to the cyclopropane requiring both the presence and
assistance of a nucleophile (SN2 mechanism). No doubt this contributes to
the DNA alkylation selectivity of this class of agents and suggests that
the positioning of an accessible nucleophile (adenine N-3) and not C-4
carbonyl protonation is the rate-determining step controlling the sequence
selectivity of the DNA alkylation reaction.
ST CBI methoxy analog prepn DNA alkylation; neoplasm inhibitor CBI methoxy
analog
IT Kinetics of solvolysis
(of methoxylated CBI analogs of CC-1065)
IT Neoplasm inhibitors
(preparation and DNA alkylation properties of methoxylated CBI analogs of
CC-1065)
IT Deoxyribonucleic acids
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(preparation and DNA alkylation properties of methoxylated CBI analogs of
CC-1065)
IT 127379-15-1 128300-13-0 132746-32-8 144732-53-6 157035-50-2

157035-51-3
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)
 (kinetics of solvolysis of)

IT 173483-67-5P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and DNA alkylation properties of methoxylated CBI analogs of CC-1065)

IT 69866-21-3DP, CC-1065, CBI analogs 173655-21-5P 173655-22-6P
 173655-25-9P 173655-26-0P 173655-27-1P 173655-28-2P 173655-29-3P
 173655-30-6P 173655-31-7P 173655-32-8P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation and DNA alkylation properties of methoxylated CBI analogs of CC-1065)

IT 173483-68-6P
 RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
 (preparation and DNA alkylation properties of methoxylated CBI analogs of CC-1065)

IT 123-25-1, Diethyl succinate 591-31-1, 3-Methoxybenzaldehyde 870-63-3
 62209-77-2 77924-28-8 101134-91-2 105518-47-6 107474-59-9
 128781-07-7
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation and DNA alkylation properties of methoxylated CBI analogs of CC-1065)

IT 151502-65-7P 151502-66-8P 157188-04-0P 173483-53-9P 173483-54-0P
 173483-55-1P 173483-56-2P 173483-57-3P 173483-58-4P 173483-59-5P
 173483-60-8P 173483-61-9P 173483-62-0P 173483-63-1P 173483-64-2P
 173483-65-3P 173483-66-4P 173483-69-7P 173483-70-0P 173483-71-1P
 173483-72-2P 173483-73-3P 173483-74-4P 173483-75-5P
173483-77-7P 173483-78-8P 173483-79-9P
 173483-81-3P 173483-85-7P 173483-86-8P 173483-87-9P 173483-90-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and DNA alkylation properties of methoxylated CBI analogs of CC-1065)

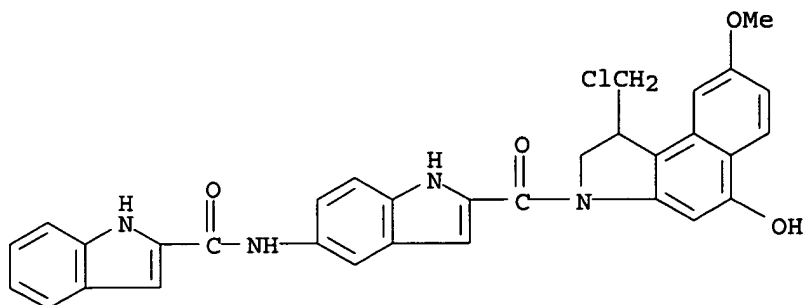
IT 173483-76-6P 173483-80-2P 173483-82-4P 173483-83-5P 173483-84-6P
 173483-88-0P 173483-89-1P 173655-23-7P 173655-24-8P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation and DNA alkylation properties of methoxylated CBI analogs of CC-1065)

IT 92191-07-6P
 RL: BYP (Byproduct); PREP (Preparation)
 (preparation of)

IT **173483-77-7P 173483-78-8P 173483-79-9P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and DNA alkylation properties of methoxylated CBI analogs of CC-1065)

IT **173483-77-7P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and DNA alkylation properties of methoxylated CBI analogs of CC-1065)

RN 173483-77-7 HCAPLUS
 CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-8-methoxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



L31 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:981710 HCAPLUS

DN 124:86653

ED Entered STN: 13 Dec 1995

TI 1,2,9,9a-Tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) analogs of CC-1065 and the duocarmycins: synthesis and evaluation

AU Boger, Dale L.; Yun, Weiya; Han, Nianhe

CS Dep. Chem., Scripps Res. Inst., La Jolla, CA, 92037, USA

SO Bioorganic & Medicinal Chemistry (1995), 3(11), 1429-53

CODEN: BMECEP; ISSN: 0968-0896

PB Elsevier

DT Journal

LA English

CC 26-6 (Biomolecules and Their Synthetic Analogs)

Section cross-reference(s): 1

AB An extensive study of analogs of the potent antitumor antibiotics CC-1065 and the duocarmycins which contain the 1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) alkylation subunit are detailed. In contrast to early speculation, deep-seated modifications in the CC-1065 and duocarmycin alkylation subunits are well tolerated and the CBI-based analogs proved to be potent cytotoxic agents and efficacious antitumor compds. Full details of studies defining a direct relationship between functional stability and in vitro cytotoxic potency are described. The readily accessible CBI-based analogs were four times more stable and four times more potent than the corresponding analogs containing the authentic CPI alkylation subunit of CC-1065 and comparable in potency to agents containing the authentic alkylation subunit of duocarmycin SA. Similarly, the CBI-based agents alkylate DNA with an unaltered sequence selectivity at an enhanced rate and with a greater efficiency than the corresponding CPI analog and were comparable to the corresponding analog incorporating the duocarmycin SA alkylation subunit. Systematic and extensive modifications and simplification in the DNA binding subunits attached to CBI were explored with the comparisons of both enantiomers of CC-1065 and the duocarmycins with enantiomers of many of the analogs.

ST cyclopropabenzindolone analog CC1065 duocarmycin prepn antitumor

IT Kinetics of solvolysis

(of cyclopropabenzindolone analogs of CC1065 and duocarmycins)

IT Neoplasm inhibitors

(preparation and antitumor evaluation of cyclopropabenzindolone analogs of CC1065 and duocarmycins)

IT 172491-26-8 172491-27-9 172491-28-0 172491-29-1 172491-30-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(preparation and antitumor evaluation of cyclopropabenzindolone analogs of CC1065 and duocarmycins)

IT 69866-21-3DP, CC-1065, cyclopropabenzindolone analogs 130288-24-3DP, Duocarmycin SA, cyclopropabenzindolone analogs 155861-67-9P

155861-68-0P 155861-69-1P 172491-22-4P 172491-23-5P 172491-25-7P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and antitumor evaluation of cyclopropabenzindolone analogs of CC1065 and duocarmycins)

IT 155861-70-4P 172375-61-0P 172375-62-1P 172375-63-2P 172375-64-3P
 172375-65-4P 172375-66-5P 172491-21-3P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and antitumor evaluation of cyclopropabenzindolone analogs of CC1065 and duocarmycins)

IT 135306-52-4P 141781-45-5P 172375-79-0P 172375-80-3P 172375-81-4P
 172375-82-5P 172375-83-6P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation and antitumor evaluation of cyclopropabenzindolone analogs of CC1065 and duocarmycins)

IT 496-41-3, 2-Benzofurancarboxylic acid 1477-50-5, 2-Indolecarboxylic acid
 6314-28-9, 2-Benzothiophenecarboxylic acid 7497-12-3,
 Bis(2,4-dinitrophenyl) carbonate 10242-12-3, 5-Nitro-2-benzofurancarboxylic acid 107474-69-1 120506-51-6 128571-50-6,
 (+)-CBI 130007-86-2 130008-89-8 147539-80-8, Methyl 5-amino-2-indolecarboxylate
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation and antitumor evaluation of cyclopropabenzindolone analogs of CC1065 and duocarmycins)

IT 1646-29-3P, Methyl 5-amino-2-benzofurancarboxylate 64512-81-8P
 101134-91-2P 104862-11-5P, Methyl 5-nitro-2-benzofurancarboxylate
 110314-42-6P 130007-88-4P 130007-89-5P **135306-53-5P**
 154272-33-0P 154272-34-1P 154272-35-2P 154294-77-6P 172375-67-6P
 172375-68-7P 172375-69-8P 172375-70-1P 172375-71-2P 172375-72-3P
172375-73-4P 172375-74-5P 172375-75-6P 172375-76-7P
 172375-77-8P 172375-78-9P 172375-84-7P 172375-85-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and antitumor evaluation of cyclopropabenzindolone analogs of CC1065 and duocarmycins)

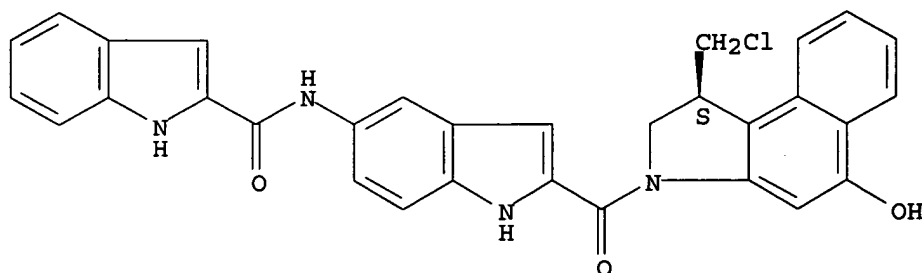
IT 172375-86-9P 172375-87-0P 172375-88-1P 172491-24-6P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation and antitumor evaluation of cyclopropabenzindolone analogs of CC1065 and duocarmycins)

IT **135306-53-5P 172375-73-4P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and antitumor evaluation of cyclopropabenzindolone analogs of CC1065 and duocarmycins)

IT **135306-53-5P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and antitumor evaluation of cyclopropabenzindolone analogs of CC1065 and duocarmycins)

RN 135306-53-5 HCAPLUS
 CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L31 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1994:235386 HCAPLUS

DN 120:235386

ED Entered STN: 14 May 1994

TI Evaluation of functional analogs of CC-1065 and the duocarmycins incorporating the crosslinking 9a-chloromethyl-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (C2BI) alkylation subunit

AU Boger, Dale L.; Johnson, Douglas S.; Palanki, Moorthy S. S.

CS Dep. Chem., Scripps Res. Inst., La Jolla, CA, 92037, USA

SO Bioorganic & Medicinal Chemistry (1993), 1(1), 27-38

CODEN: BMECEP; ISSN: 0968-0896

DT Journal

LA English

CC 1-3 (Pharmacology)

AB The DNA alkylation properties and in vitro cytotoxic activity of a series of analogs of CC-1065 and the duocarmycins incorporating the 9a-chloromethyl-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (C2BI) alkylation subunit are detailed. The C2BI-based agents have been shown to alkylate DNA within the minor groove in a fashion analogous to CC-1065 or duocarmycin. The stereoelectronically controlled adenine N3 addition to the least substituted cyclopropane carbon occurs with a selectivity that represents a composite of the two enantiomers of the corresponding CBI-based agents. Addnl. high-affinity alkylation sites were detected which were not prominent alkylation sites for either enantiomer of the CBI-based agents. Such sites may represent induced high-affinity alkylation sites resulting from DNA crosslinking following complementary strand alkylation at a high-affinity alkylation site and each such site detected proved consistent with predicted models of an adenine--adenine crosslinking event. Further, consistent with this interpretation, the C2BI agents were shown to constitute efficient crosslinking agents with DNA crosslinking being observed at the same concns. as DNA alkylation. In comparison to the parent CBI-based agents, the C2BI-based agents proved to be approx. 100-10,000x less effective at DNA alkylation and 100-10,000x less potent in cytotoxic assays. This is suggested to be the consequence of a significant steric deceleration of the adenine N3 alkylation reaction attributable to the addnl. 9a-chloromethyl substituent. Consistent with this interpretation, the noncovalent binding constant of C2BI-CDPI2 for poly[dA]-poly[dT] proved nearly identical to that of CDPI3 under kinetic binding conditions, and prolonged incubation of C2BI-CDPI2 with poly[dA]-poly[dT] (72 h, 25°) provided covalent complexes with a helix stabilization comparable to that observed with (+)- or (-)-CPI-CDPI2 indicating that the size of the C2BI subunit inhibits but does not preclude productive DNA alkylation.

ST CC1065 duocarmycin DNA crosslinking chloromethyltetrahydrocyclopropabenzindolone alkylation

IT Cytotoxic agents

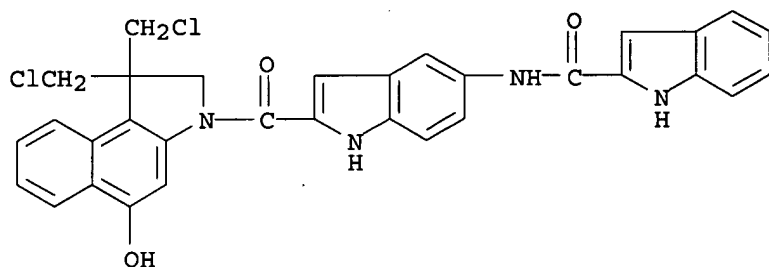
(CC-1065 and duocarmycin analogs as, DNA crosslinking by)

IT Deoxyribonucleic acids

RL: BIOL (Biological study)

(crosslinking, from CC-1065 and duocarmycin analogs, cytotoxicity in relation to)

- IT Molecular structure-biological activity relationship
(DNA-crosslinking, of CC-1065 and duocarmycin analogs)
- IT Molecular structure-biological activity relationship
(cytotoxic, of CC-1065 and duocarmycin analogs)
- IT 69866-21-3D, CC-1065, analogs 118292-34-5D, Duocarmycin A, analogs
144318-47-8 144318-48-9 144318-50-3 144318-51-4 144318-52-5
144318-54-7 144318-55-8 144318-56-9 144318-57-0 144318-58-1
144318-59-2 **144318-60-5** 144318-61-6 154497-13-9
RL: BIOL (Biological study)
(DNA alkylation and cytotoxic activities of, incorporating the crosslinking chloromethyltetrahydrocyclopropa[c]benz[e]indolone alkylation subunit)
- IT **144318-60-5**
RL: BIOL (Biological study)
(DNA alkylation and cytotoxic activities of, incorporating the crosslinking chloromethyltetrahydrocyclopropa[c]benz[e]indolone alkylation subunit)
- IT **144318-60-5**
RL: BIOL (Biological study)
(DNA alkylation and cytotoxic activities of, incorporating the crosslinking chloromethyltetrahydrocyclopropa[c]benz[e]indolone alkylation subunit)
- RN 144318-60-5 HCAPLUS
- CN 1H-Indole-2-carboxamide, N-[2-[[1,1-bis(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



- L31 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
- AN 1992:651104 HCAPLUS
- DN 117:251104
- ED Entered STN: 26 Dec 1992
- TI Functional analogs of CC-1065 and the duocarmycins incorporating the 9a-(chloromethyl)-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (C2BI) alkylation subunit: synthesis and preliminary DNA alkylation studies
- AU Boger, Dale L.; Palanki, Moorthy S. S.
- CS Dep. Chem., Scripps Res. Inst., La Jolla, CA, 92037, USA
- SO Journal of the American Chemical Society (1992), 114(24), 9318-27
CODEN: JACSAT; ISSN: 0002-7863
- DT Journal
- LA English
- CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1
- OS CASREACT 117:251104
- GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

- AB A concise and effective nine to ten step synthesis of 9a-(chloromethyl)-1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (I) is detailed based on the implementation of a key 5-exo-trig aryl radical-alkene cyclization for direct introduction of a selectively protected 3,3-bis(hydroxymethyl)indoline. The incorporation of I into functional analogs of CC-1065 and the duocarmycins is described. The fundamental solvolytic behavior of N-tert-butoxycarbonyl-I is detailed ($t_{1/2}$ = 433 h, pH = 3) in studies which reveal that the agent is approx. 12 times more stable than the authentic alkylation subunit of CC-1065 and that it participates in the stereoelectronically-controlled reaction with nucleophilic addition to the least substituted cyclopropane carbon. Preliminary studies demonstrating the DNA alkylation and crosslinking properties of benzindole II (R = Q) and cyclopropabenzindole III (R = Q) are presented.
- ST CC1065 cyclopropabenzindolone analog; chloromethylbenzindole analog
CC1065; crosslinking DNA CC1065 cyclopropabenzindolone analog; DNA alkylation CC1065 cyclopropabenzindolone analog
- IT Deoxyribonucleic acids
RL: PRP (Properties)
(alkylation and crosslinking of, with chloromethylcyclopropabenzindole analogs of CC-1065)
- IT 56061-88-2 144345-49-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(Wittig reaction of, with phenylaminomethyl benzyloxymethyl ketone)
- IT 101134-91-2 105518-47-6 107474-59-9 128781-07-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation reaction of, with chloromethylbenzindole)
- IT 144318-53-6P
RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(formation and amidation of, with indolecarboxylic acids)
- IT 69866-21-3DP, CC-1065, chloromethylcyclopropabenzindole analogs
RL: PREP (Preparation)
(preparation and DNA alkylation and crosslinking by)
- IT 144318-57-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and DNA alkylation and crosslinking by)
- IT 144318-34-3P 144318-41-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and Wittig reaction of, with pyraniloxy methylenephosphorane)
- IT 22539-93-1P, 1-(Benzyloxy)propan-2-one 144318-39-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and bromination of)
- IT 144318-46-7P 144318-49-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and chlorination of)
- IT 144318-42-3P 144318-43-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, benzindole from)
- IT 144318-47-8P 144318-50-3P 144318-54-7P 144318-58-1P
144318-60-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, cyclopropabenzindolone from)
- IT 144318-35-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, indoline from)

IT 144318-37-6P 144318-45-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and debenzylation of)

IT 144318-36-5P 144318-44-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and detetrahydropyranylation of)

IT 4039-82-1P, Benzyl propargyl ether
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and oxidation of, benzyloxymethyl Me ketone from)

IT 144318-51-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and solvolytic reactivity of)

IT 144318-40-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and N-alkylation of, with benzyloxymethyl bromomethyl ketone)

IT 1024-38-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and N-alkylation of, with bromomethyl benzyloxymethyl ketone)

IT 144318-38-7P 144318-48-9P 144318-52-5P 144318-55-8P 144318-59-2P
144318-61-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 144318-56-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, cyclization of, and DNA alkylation and crosslinking by)

IT 106-96-7, Propargyl bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(substitution reaction of, with benzyl alc.)

IT 100-51-6, Benzyl alcohol, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(substitution reaction of, with propargyl bromide)

IT 615-36-1, 2-Bromoaniline 122745-35-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(tosylation of)

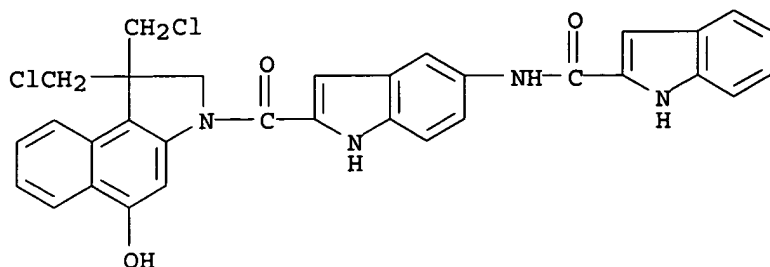
IT 144318-33-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-alkylation by, of tosylation and tosylaminonaphthalene)

IT 144318-60-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, cyclopropabenzindolone from)

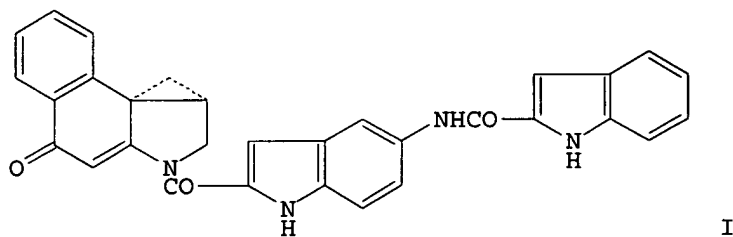
IT 144318-60-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, cyclopropabenzindolone from)

RN 144318-60-5 HCAPLUS

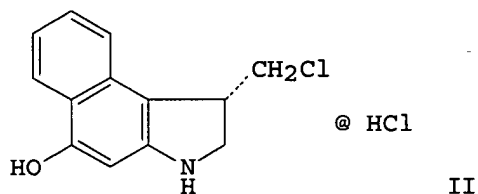
CN 1H-Indole-2-carboxamide, N-[2-[[1,1-bis(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)



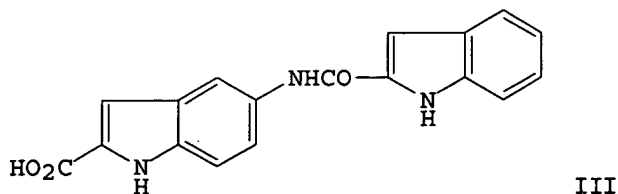
L31 ANSWER 20 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1991:491913 HCAPLUS
 DN 115:91913
 ED Entered STN: 06 Sep 1991
 TI Synthesis and preliminary evaluation of (+)-CBI-indole2: an enhanced functional analog of (+)-CC-1065.
 AU Boger, Dale L.; Ishizaki, Takayoshi; Sakya, Subas M.; Munk, Stephen A.; Kitos, Paul A.; Jin, Qing; Besterman, Jeffrey M.
 CS Dep. Chem., Purdue Univ., West Lafayette, IN, 47907, USA
 SO Bioorganic & Medicinal Chemistry Letters (1991), 1(2), 115-20
 CODEN: BMCLE8; ISSN: 0960-894X
 DT Journal
 LA English
 CC 26-6 (Biomolecules and Their Synthetic Analogs)
 Section cross-reference(s): 1
 GI



I



II

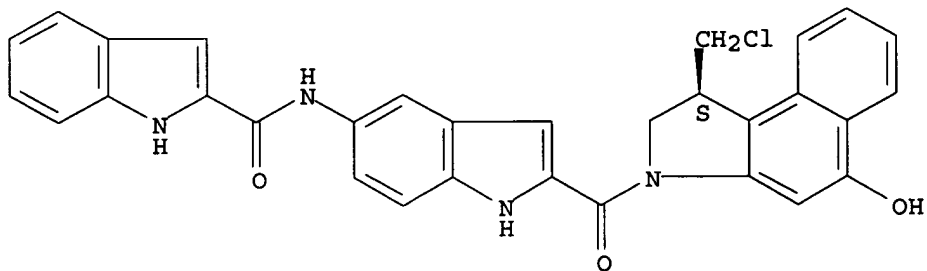


III

AB The title compound (I) was prepared from the chloromethylbenzindole II and the indolecarboxamidoindolecarboxylic acid III. I has better antitumor activity than its pyrroloindole analog.

ST cyclopropabenzindole fragment CC 1065; antitumor CC 1065 fragment
 IT Neoplasm inhibitors
 (cyclopropabenzindolone fragment of CC-1065)
 IT 101222-80-4
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (antitumor activity of)
 IT 69866-21-3P, (+)-CC 1065
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (cyclopropabenzindole fragment of, preparation and antitumor activity of)
 IT 130007-86-2
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (deblocking of)
 IT 135306-52-4P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation and antitumor activity of)
 IT 135306-53-5P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and cyclopropanation of)
 IT 130007-89-5P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and reaction of, with indolecarboxamidoleindolecarboxylic acid)
 IT 101134-91-2
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with chloromethylbenzindole)
 IT 135306-53-5P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and cyclopropanation of)
 IT 135306-53-5P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and cyclopropanation of)
 RN 135306-53-5 HCAPLUS
 CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



=> fil uspatall

FILE 'USPATFULL' ENTERED AT 15:56:47 ON 29 SEP 2004

CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 15:56:47 ON 29 SEP 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> => d l37 bib abs hitrn fhitstr tot

L37 ANSWER 1 OF 12 USPATFULL on STN

AN 2004:144203 USPATFULL

TI Prodrugs of CC-1065 analogs

IN Yongxin, Robert, Watertown, MA, UNITED STATES

Chari, Ravi V.J., Newton, MA, UNITED STATES

PA IMMUNOGEN INC. (U.S. corporation)

PI US 2004109867 A1 20040610

AI US 2003-692856 A1 20031027 (10)

RLI Division of Ser. No. US 2002-116053, filed on 5 Apr 2002, PENDING

DT Utility

FS APPLICATION

LREP SUGHRUE MION, PLLC, 2100 PENNSYLVANIA AVENUE, N.W., SUITE 800,
WASHINGTON, DC, 20037

CLMN Number of Claims: 28

ECL Exemplary Claim: 1

DRWN 7 Drawing Page(s)

LN.CNT 1134

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Prodrugs of analogs of the anti-tumor antibiotic CC-1065 having a cleavable protective group such as a piperazino carbamate, a 4-piperidino-piperidino carbamate or a phosphate, in which the protecting group confers enhanced water solubility and stability upon the prodrug, and in which the prodrug also has a moiety, such as a disulfide, that can conjugate to a cell binding reagent such as an antibody. The therapeutic use of such prodrug conjugates is also described; such prodrugs of cytotoxic agents have therapeutic use because they can deliver cytotoxic prodrugs to a specific cell population for enzymatic conversion to cytotoxic drugs in a targeted fashion.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 501441-05-0P 501666-85-9P 615538-42-6P

615538-45-9P 615538-47-1P 615538-49-3P

(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT 615538-44-8P 615538-46-0P 615538-48-2P

(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT 615538-51-7P 615538-52-8P

(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT 615538-53-9P 615538-54-0P 615538-55-1P

615538-56-2P 615538-57-3DP, salt 615538-58-4P

615538-59-5DP, salt

(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

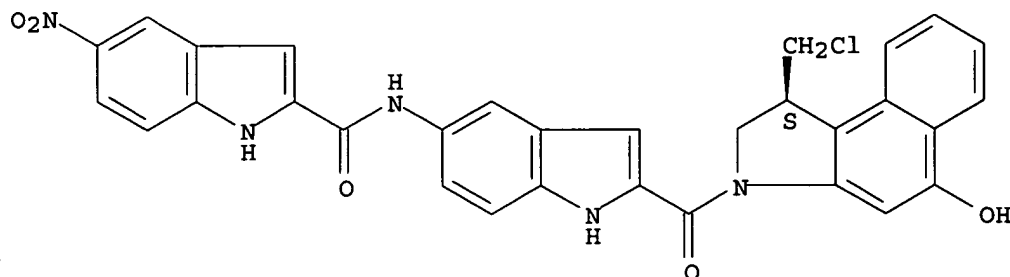
IT 501441-05-0P

(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

RN 501441-05-0 USPATFULL

CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-nitro- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



L37 ANSWER 2 OF 12 USPATFULL on STN

AN 2004:44969 USPATFULL

TI Novel prodrugs von 6-hydroxy-2,3-dihydro-1h-indoles, 5-hydroxy-1,2-dihydro-3h-pyrrolo[3,2-e]indoles and 5-hydroxy-1,2-dihydro-3h-benzo(e)indoles as well as of 6-hydroxy-1,2,3,4-tetrahydro-benzo[f]quinoline derivatives for use in selective cancer therapy

IN Tietze, Lutz F., Gottingen, GERMANY, FEDERAL REPUBLIC OF
Herzig, Tobias, Marsstr, GERMANY, FEDERAL REPUBLIC OF
Fecher, Anja, Eisenbahnstr.16, GERMANY, FEDERAL REPUBLIC OF

PI US 2004033962 A1 20040219

AI US 2003-275415 A1 20030630 (10)

WO 2001-EP4904 20010502

PRAI DE 2000-100 20000502

DE 2000-100 20000523

DT Utility

FS APPLICATION

LREP Stephan A Pendorff, Pendorff & Cutliff, PO Box 20445, Tampa, FL,
33622-0445

CLMN Number of Claims: 10

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1047

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The chemotherapy of malignant tumours is greatly restricted by the generally slight differentiation of the available cytostatic agents between normal and malignant tissue. In order to achieve an improvement of the selectivity in cancer therapy, novel prodrugs have been developed from 6-hydroxy-2,3-dihydro-1H-indolene, 5-hydroxy-1,2-dihydro-3H-pyrrolo[3,2-e]indolene and 5-hydroxy-1,2-dihydro-3H-benzo[e]indolene as well as from 6-hydroxy-1,2,3,4-tetrahydro-benzo[f]-quinolines, that may be used within the framework of the ADEP therapy (antibody directed enzyme prodrug therapy). The new prodrugs are characterised by a high difference in toxicity between the prodrug and underlying drug and by a very high efficacy of the drug. The high selectivity of the new prodrugs is probably attributed to the fact that, in the new prodrugs, a secondary halide is present in contrast to the prodrugs of a similar type previously produced by us. The direct alkylation of the DNA or RNA by the prodrugs and thus the toxicity of the prodrugs is thereby reduced. After splitting off of the glycosidic and/or acetal group on the phenolic hydroxy groups of the prodrugs, a spirocyclopropacyclohexadiene is formed which, being a highly toxic group, effects an alkylation of the DNA or RNA.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 330206-90-1P

(preparation of glycosidic prodrugs containing substituted indolenes for use in cancer therapy)

IT 330206-89-8P

(preparation of glycosidic prodrugs containing substituted indolenes for
use in cancer therapy)

IT 330206-90-1P

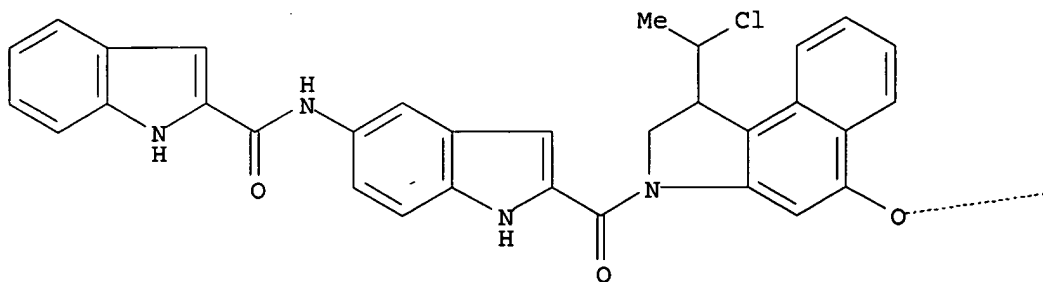
(preparation of glycosidic prodrugs containing substituted indolenes for
use in cancer therapy)

RN 330206-90-1 USPATFULL

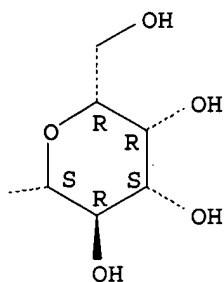
CN 1H-Indole-2-carboxamide, N-[2-[[1-(1-chloroethyl)-5-(β -D-galactopyranosyloxy)-1,2-dihydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L37 ANSWER 3 OF 12 USPATFULL on STN

AN 2004:2505 USPATFULL

TI CBI analogs of CC-1065 and the duocarmycins

IN Boger, Dale L., La Jolla, CA, UNITED STATES

PA The Scripps Research Institute, La Jolla, CA, UNITED STATES (U.S. corporation)

PI US 2004002528 A1 20040101

AI US 2003-417043 A1 20030415 (10)

RLI Continuation of Ser. No. US 1998-51264, filed on 2 Oct 1998, GRANTED, Pat. No. US 6548530 A 371 of International Ser. No. WO 1996-US16481, filed on 3 Oct 1996, PENDING

PRAI US 1995-4752P 19951003 (60)

DT Utility

FS APPLICATION

LREP THE SCRIPPS RESEARCH INSTITUTE, OFFICE OF PATENT COUNSEL, TPC-8, 10550 NORTH TORREY PINES ROAD, LA JOLLA, CA, 92037

CLMN Number of Claims: 24

ECL Exemplary Claim: 1

DRWN 34 Drawing Page(s)

LN.CNT 2984

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Analog of the antitumor antibiotics CC-1065 and the duocarmycins incorporate the 1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) alkylation subunit. The CBI-based analogs have potent cytotoxic activity and are useful as efficacious antitumor compounds. A direct relationship between functional stability and in vitro cytotoxic potency is disclosed. The CBI-based analogs are easily synthesized and are 4+ more stable and 4+ more potent than the corresponding analogs containing the authentic CPI alkylation subunit of CC-1065 and comparable in potency to agents containing the authentic alkylation subunit of duocarmycin SA. Similarly, the CBI-based agents alkylate DNA with an unaltered sequence selectivity at an enhanced rate and with a greater efficiency than the corresponding CPI analog and were comparable to the corresponding analog incorporating the duocarmycin SA alkylation subunit. Systematic and extensive modifications and simplifications in the DNA binding subunits attached to CBI are also described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 135306-53-5P 172375-73-4P

(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

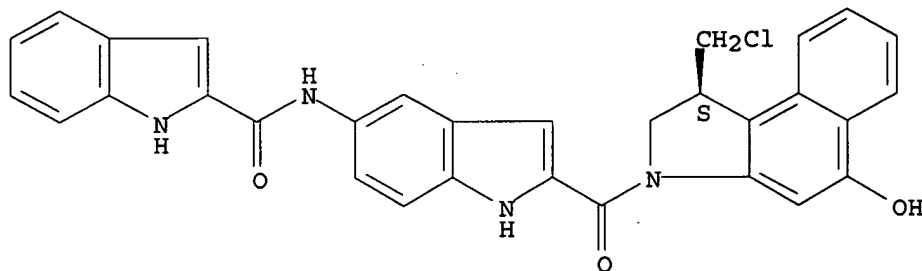
IT 135306-53-5P

(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

RN 135306-53-5 USPATFULL

CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L37 ANSWER 4 OF 12 USPATFULL on STN

AN 2003:283175 USPATFULL

TI Prodrugs of CC-1065 analogs

IN Zhao, Robert Yongxin, Watertown, MA, UNITED STATES

Chari, Ravi V.J., Newton, MA, UNITED STATES

PA IMMUNOGEN INC. (U.S. corporation)

PI US 2003199519 A1 20031023

US 6756397 B2 20040629

AI US 2002-116053 A1 20020405 (10)

DT Utility

FS APPLICATION

LREP SUGHRUE MION, PLLC, 2100 Pennsylvania Avenue, NW, Washington, DC, 20037-3213

CLMN Number of Claims: 28

ECL Exemplary Claim: 1

DRWN 7 Drawing Page(s)

LN.CNT 1140

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Prodrugs of analogs of the anti-tumor antibiotic CC-1065 having a cleavable protective group such as a piperazino carbamate, a

4-piperidino-piperidino carbamate or a phosphate, in which the protecting group confers enhanced water solubility and stability upon the prodrug, and in which the prodrug also has a moiety, such as a disulfide, that can conjugate to a cell binding reagent such as an antibody. The therapeutic use of such prodrug conjugates is also described; such prodrugs of cytotoxic agents have therapeutic use because they can deliver cytotoxic prodrugs to a specific cell population for enzymatic conversion to cytotoxic drugs in a targeted fashion.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 501441-05-0P 501666-85-9P 615538-42-6P
615538-45-9P 615538-47-1P 615538-49-3P
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT 615538-44-8P 615538-46-0P 615538-48-2P
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT 615538-51-7P 615538-52-8P
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

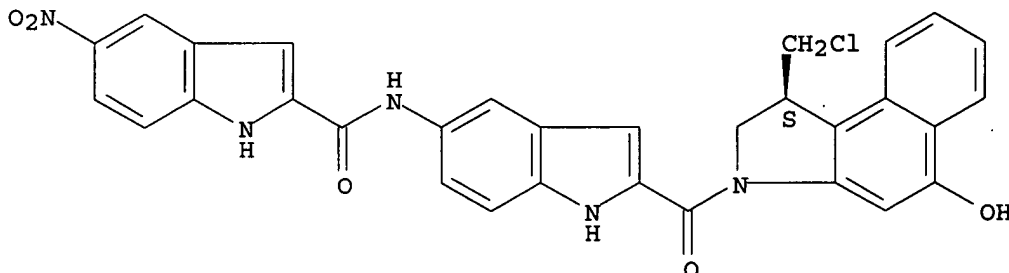
IT 615538-53-9P 615538-54-0P 615538-55-1P
615538-56-2P 615538-57-3DP, salt 615538-58-4P
615538-59-5DP, salt
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT 501441-05-0P
(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

RN 501441-05-0 USPATFULL

CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-nitro- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



L37 ANSWER 5 OF 12 USPATFULL on STN

AN 2003:277338 USPATFULL

TI CC-1065 analog synthesis

IN Zhao, Robert Yongxin, Watertown, MA, UNITED STATES
Chari, Ravi V.J., Newton, MA, UNITED STATES

PA IMMUNOGEN INC. (U.S. corporation)

PI US 2003195365 A1 20031016

AI US 2002-265452 A1 20021007 (10)

RLI Division of Ser. No. US 2002-116052, filed on 5 Apr 2002, GRANTED, Pat.
No. US 6534660

DT Utility

FS APPLICATION

LREP SUGHRUE MION, PLLC, 2100 PENNSYLVANIA AVENUE, N.W., WASHINGTON, DC,
20037

CLMN Number of Claims: 17

ECL Exemplary Claim: 1

DRWN 3 Drawing Page(s)

LN.CNT 890

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Improved synthesis of seco(-)CBI (5-hydroxy-3-amino-1-[S]-(chloromethyl)-1,2-dihydro-3H-benz(e)indole): ##STR1##

and improved syntheses therefrom of a wide variety of CC-1065 analogs that comprise a cyclopropabenzidole (CBI) alkylating moiety, and which are collectively DC1 and its derivatives, for the synthesis of cell-targeted therapeutic agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 501441-05-0P, 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole (intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

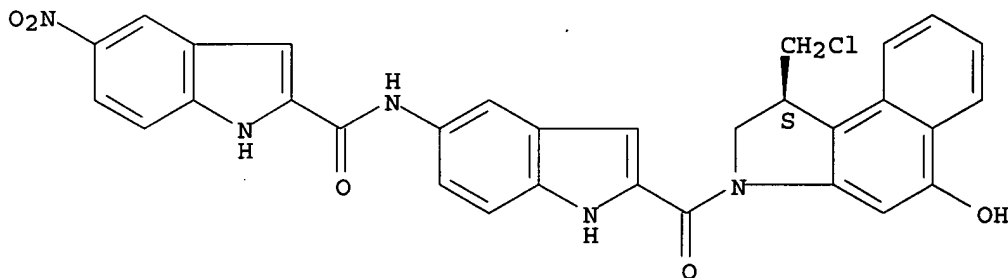
IT 501666-85-9P 501666-87-1P (target product; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT 501441-05-0P, 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole (intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

RN 501441-05-0 USPATFULL

CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L37 ANSWER 6 OF 12 USPATFULL on STN

AN 2003:176513 USPATFULL

TI CC-1065 analog synthesis

IN Zhao, Robert Yongxin, Watertown, MA, United States

Chari, Ravi V. J., Newton, MA, United States

PA Immunogen Inc., Cambridge, MA, United States (U.S. corporation)

PI US 6586618 B1 20030701

AI US 2002-265329 20021007 (10)

RLI Division of Ser. No. US 2002-116052, filed on 5 Apr 2002

DT Utility

FS GRANTED

EXNAM Primary Examiner: McKane, Joseph K.; Assistant Examiner: Saeed, Kamal

LREP Sughrue Mion, PLLC

CLMN Number of Claims: 2

ECL Exemplary Claim: 1

DRWN 3 Drawing Figure(s); 3 Drawing Page(s)

LN.CNT 837

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Improved synthesis of seco(-)CBI (5-hydroxy-3-amino-1-[S]-(chloromethyl)-1,2-dihydro-3H-benz(e)indole): ##STR1##

and improved syntheses therefrom of a wide variety of CC-1065 analogs that comprise a cyclopropabenzidole (CBI) alkylating moiety, and which

are collectively DC1 and its derivatives, for the synthesis of cell-targeted therapeutic agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 501441-05-0P, 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole (intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

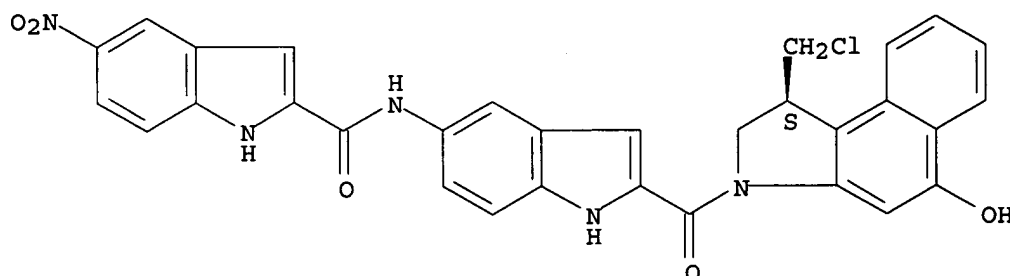
IT 501666-85-9P 501666-87-1P (target product; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

IT 501441-05-0P, 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole (intermediate; preparation of seco(-)CBI as an intermediate in synthesis of CC-1065 analogs)

RN 501441-05-0 USPATFULL

CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L37 ANSWER 7 OF 12 USPATFULL on STN

AN 2003:102391 USPATFULL

TI CBI analogs of CC-1065 and the duocarmycins

IN Boger, Dale L., La Jolla, CA, United States

PA The Scripps Research Institute, La Jolla, CA, United States (U.S. corporation)

PI US 6548530 B1 20030415

WO 9712862 19970410

AI US 1998-51264 19981002 (9)

WO 1996-US16481 19961003

PRAI US 1995-4752P 19951003 (60)

DT Utility

FS GRANTED

EXNAM Primary Examiner: Stockton, Laura L.

LREP Lewis, Donald G.

CLMN Number of Claims: 7

ECL Exemplary Claim: 1

DRWN 41 Drawing Figure(s); 34 Drawing Page(s)

LN.CNT 2950

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Analogs of the antitumor antibiotics CC-1065 and the duocarmycins incorporate the 1,2,9,9a-tetrahydrocyclopropa[c]benz[e]indol-4-one (CBI) alkylation subunit. The CBI-based analogs have potent cytotoxic activity and are useful as efficacious antitumor compounds. A direct relationship between functional stability and in vitro cytotoxic potency is disclosed. The CBI-based analogs are easily synthesized and are 4+ more stable and 4+ more potent than the corresponding analogs containing the authentic CPI alkylation subunit of CC-1065 and

comparable in potency to agents containing the authentic alkylation subunit of duocarmycin SA. Similarly, the CBI-based agents alkylate DNA with an unaltered sequence selectivity at an enhanced rate and with a greater efficiency than the corresponding CPI analog and were comparable to the corresponding analog incorporating the duocarmycin SA alkylation subunit. Systematic and extensive modifications and simplifications in the DNA binding subunits attached to CBI are also described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 135306-53-5P 172375-73-4P

(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

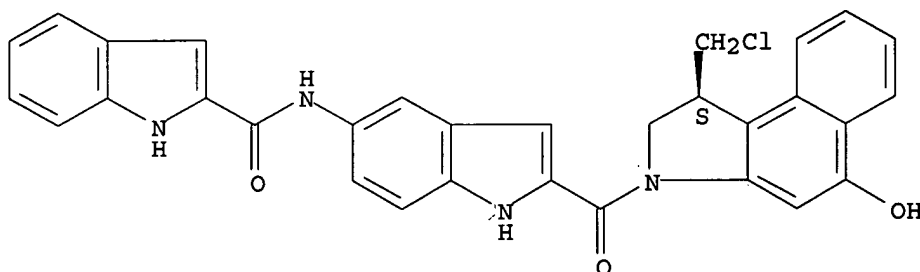
IT 135306-53-5P

(preparation of analogs of CC-1065 and the duocarmycins, containing the cyclopropa[c]benz[e]indol-4-one subunit, for use as antitumor agents)

RN 135306-53-5 USPATFULL

CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L37 ANSWER 8 OF 12 USPATFULL on STN

AN 2003:74493 USPATFULL

TI CC-1065 analog synthesis

IN Yongxin, Robert, Watertown, MA, United States

Chari, Ravi V. J., Newton, MA, United States

PA Immunogen, Inc., Cambridge, MA, United States (U.S. corporation)

PI US 6534660 B1 20030318

AI US 2002-116052 20020405 (10)

DT Utility

FS GRANTED

EXNAM Primary Examiner: McKane, Joseph K.; Assistant Examiner: Murphy, Jennifer C.

LREP Sughrue Mion, PLLC

CLMN Number of Claims: 9

ECL Exemplary Claim: 1

DRWN 3 Drawing Figure(s); 3 Drawing Page(s)

LN.CNT 851

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Improved synthesis of seco(-)CBI (5-hydroxy-3-amino-1-[S]-(chloromethyl)-1,2 -dihydro-3H-benz(e)indole): ##STR1##

and improved syntheses therefrom of a wide variety of CC-1065 analogs that comprise a cyclopropabenzidole (CBI) alkylating moiety, and which are collectively DC1 and its derivatives, for the synthesis of cell-targeted therapeutic agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 501441-05-0P, 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[[(5-nitroindol-2-

yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole
(intermediate; preparation of seco(-)CBI as an intermediate in synthesis of
CC-1065 analogs)

IT 501666-85-9P 501666-87-1P

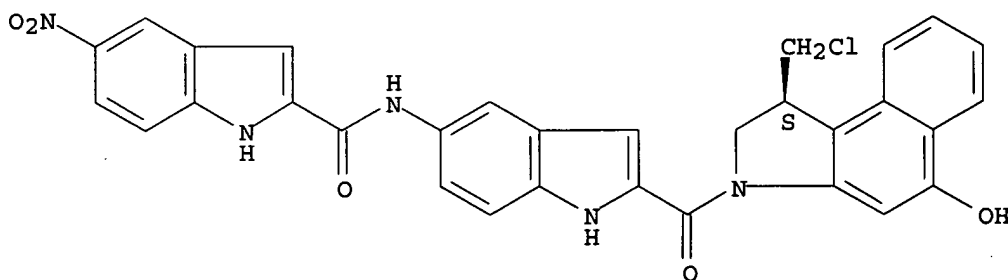
(target product; preparation of seco(-)CBI as an intermediate in synthesis
of CC-1065 analogs)

IT 501441-05-0P, 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[[5-nitroindol-
2-yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole
(intermediate; preparation of seco(-)CBI as an intermediate in synthesis of
CC-1065 analogs)

RN 501441-05-0 USPATFULL

CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-
hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-nitro- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



L37 ANSWER 9 OF 12 USPATFULL on STN

AN 2000:57902 USPATFULL

TI Analogs of CC-1065 and the duocarmycins

IN Boger, Dale L., La Jolla, CA, United States

PA The Scripps Research Institute, La Jolla, CA, United States (U.S.
corporation)

PI US 6060608 20000509

WO 9745411 19971204

AI US 1999-194467 19990907 (9)

WO 1997-US9076 19970530

19990907 PCT 371 date

19990907 PCT 102(e) date

PRAI US 1996-18860P 19960531 (60)

US 1996-23346P 19960912 (60)

DT Utility

FS Granted

EXNAM Primary Examiner: Stockton, Laura L.

LREP Lewis, Donald G.

CLMN Number of Claims: 7

ECL Exemplary Claim: 1

DRWN 45 Drawing Figure(s); 35 Drawing Page(s)

LN.CNT 3201

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Analogs of antitumor antibiotics CC-1065 and the duocarmycins are
synthesized which possess systematic and extensive modifications in the
DNA binding subunits attached to a 1,2,9,9a-tetra-hydro-cyclo-
propa[c]benz[e]indol-4-one (CBI) alkylation subunit. The analogs have
potent cytotoxic activity and are efficacious antitumor compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 178877-33-3P 178877-34-4P

(synthesis and cytotoxic activity of analogs of CC-1065 and the
duocarmycins)

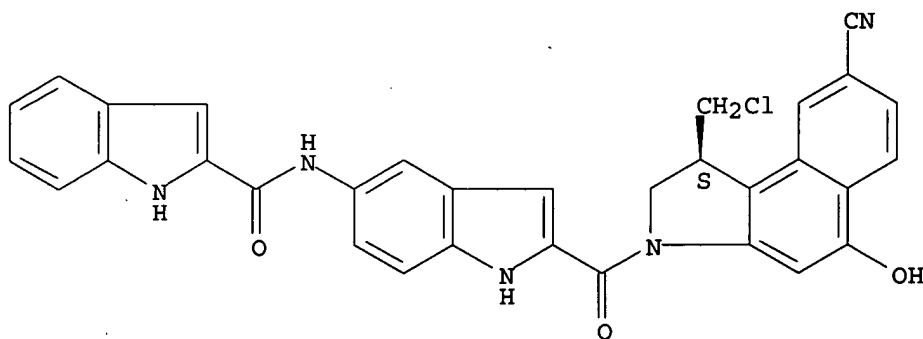
IT 178877-33-3P

(synthesis and cytotoxic activity of analogs of CC-1065 and the duocarmycins)

RN 178877-33-3 USPATFULL

CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-8-cyano-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L37 ANSWER 10 OF 12 USPATFULL on STN

AN 1999:146607 USPATFULL

TI MCBI analogs of CC-1065 and the duocarmycins

IN Boger, Dale L., La Jolla, CA, United States

PA The Scripps Research Institute, La Jolla, CA, United States (U.S. corporation)

PI US 5985908 19991116

WO 9732850 19970912

AI US 1998-142337 19980904 (9)

WO 1997-US3641 19970307

19980904 PCT 371 date

19980904 PCT 102(e) date

PRAI US 1996-13024P 19960308 (60)

DT Utility

FS Granted

EXNAM Primary Examiner: Gerstl, Robert

LREP Lewis, Donald G.

CLMN Number of Claims: 11

ECL Exemplary Claim: 1

DRWN 18 Drawing Figure(s); 20 Drawing Page(s)

LN.CNT 1985

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB MCBI (7-methoxy-1,2,9a-tetra-hydrocyclopropa[c]benz[e]indol-4-one) is employable as a DNA alkylating agent and can be incorporated into analogs of CC-1065 and the duocarmycins for constructing regioselective DNA alkylating agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 173483-78-8P

(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)

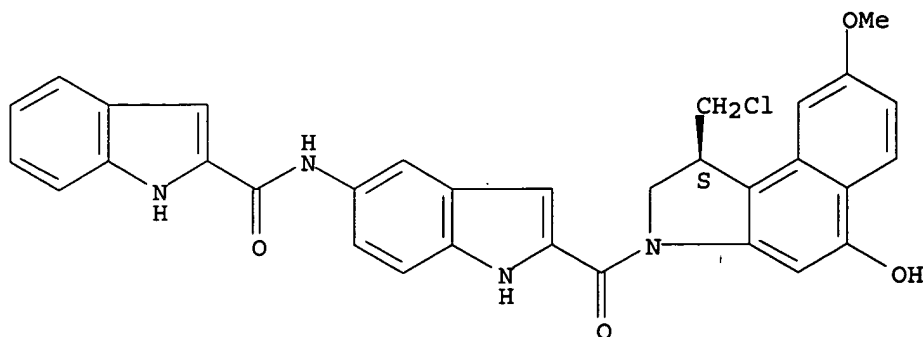
IT 173483-78-8P

(synthesis and DNA alkylating activity of MCBI analogs of CC-1065 and the duocarmycins)

RN 173483-78-8 USPATFULL

CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-8-methoxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L37 ANSWER 11 OF 12 USPATFULL on STN

AN 1998:150939 USPATFULL

TI DNA-binding indole derivatives, their prodrugs and immunoconjugates as anticancer agents

IN Wang, Yuqiang, Mountain View, CA, United States

Wright, Susan C., Saratoga, CA, United States

Larrick, James W., Woodside, CA, United States

PA Panorama Research, Inc., Mountain View, CA, United States (U.S. corporation)

PI US 5843937 19981201

AI US 1996-652883 19960523 (8)

DT Utility

FS Granted

EXNAM Primary Examiner: Raymond, Richard L.

LREP Townsend and Townsend and Crew LLP

CLMN Number of Claims: 41

ECL Exemplary Claim: 1

DRWN 11 Drawing Figure(s); 14 Drawing Page(s)

LN.CNT 1644

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to novel DNA alkylating agents and the prodrugs of these agents which are useful as antitumor agents and DNA labelling agents. The compounds are hydroxy dihydrobenzindole oligopeptides and prodrugs thereof wherein the monomeric constituents are derived from monocyclic or bicyclic heterocyclic aromatic residues.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 199806-33-2P 199806-38-7P 199806-39-8P

199806-41-2P 199806-42-3P 199806-61-6P

199806-62-7DP, monoclonal antibody conjugate 199806-64-9P

199806-65-0P

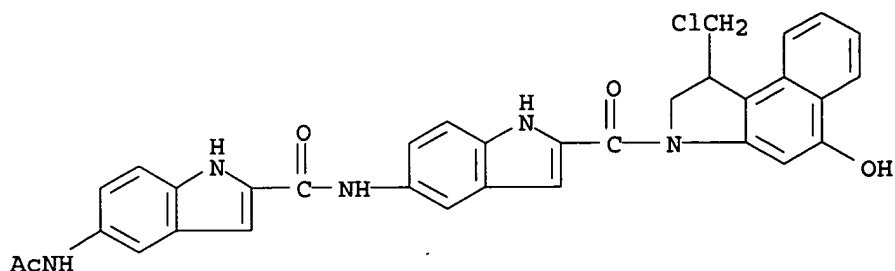
(preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

IT 199806-33-2P

(preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

RN 199806-33-2 USPATFULL

CN 1H-Indole-2-carboxamide, 5-(acetlamino)-N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI)
(CA INDEX NAME)



L37 ANSWER 12 OF 12 USPAT2 on STN

AN 2003:283175 USPAT2

TI Prodrugs of CC-1065 analogs

IN Zhao, Robert Yongxin, Watertown, MA, United States

Chari, Ravi V. J., Newton, MA, United States

PA Immunogen, Inc., Cambridge, MA, United States (U.S. corporation)

PI US 6756397 B2 20040629

AI US 2002-116053 20020405 (10)

DT Utility

FS GRANTED

EXNAM Primary Examiner: Desai, R; Assistant Examiner: Shiao, Robert

LREP Sughrue Mion, PLLC

CLMN Number of Claims: 5

ECL Exemplary Claim: 1

DRWN 9 Drawing Figure(s); 7 Drawing Page(s)

LN.CNT 1086

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Prodrugs of analogs of the anti-tumor antibiotic CC-1065 having a cleavable protective group such as a piperazino carbamate, a 4-piperidino-piperidino carbamate or a phosphate, in which the protecting group confers enhanced water solubility and stability upon the prodrug, and in which the prodrug also has a moiety, such as a disulfide, that can conjugate to a cell binding reagent such as an antibody. The therapeutic use of such prodrug conjugates is also described; such prodrugs of cytotoxic agents have therapeutic use because they can deliver cytotoxic prodrugs to a specific cell population for enzymatic conversion to cytotoxic drugs in a targeted fashion.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 501441-05-0P 501666-85-9P 615538-42-6P

615538-45-9P 615538-47-1P 615538-49-3P

(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT 615538-44-8P 615538-46-0P 615538-48-2P

(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT 615538-51-7P 615538-52-8P

(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

IT 615538-53-9P 615538-54-0P 615538-55-1P

615538-56-2P 615538-57-3DP, salt 615538-58-4P

615538-59-5DP, salt

(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

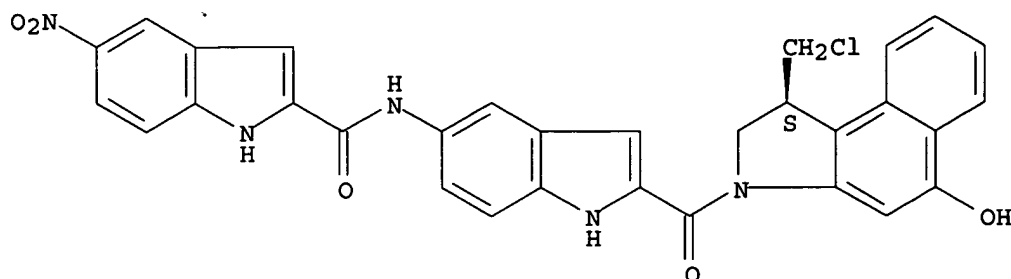
IT 501441-05-0P

(preparation of prodrugs of antibiotic CC-1065 analogs for tumor targeting)

RN 501441-05-0 USPAT2

CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-nitro- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



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STRUCTURE FILE UPDATES: 28 SEP 2004 HIGHEST RN 753424-73-6

DICTIONARY FILE UPDATES: 28 SEP 2004 HIGHEST RN 753424-73-6

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<http://www.cas.org/ONLINE/DBSS/registryss.html>

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L26 ANSWER 1 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 743424-19-3 REGISTRY

CN INDEX NAME NOT YET ASSIGNED

FS STEREOSEARCH

MF C92 H98 Cl N23 O27 S

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

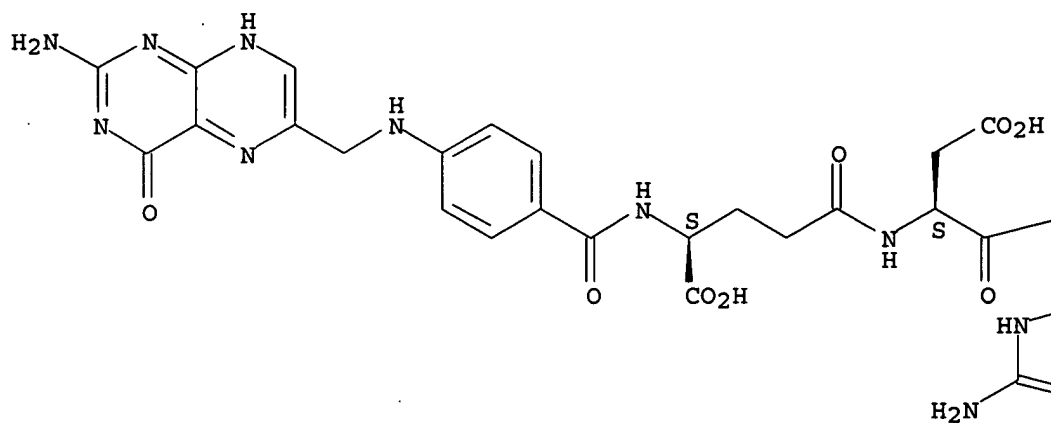
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RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

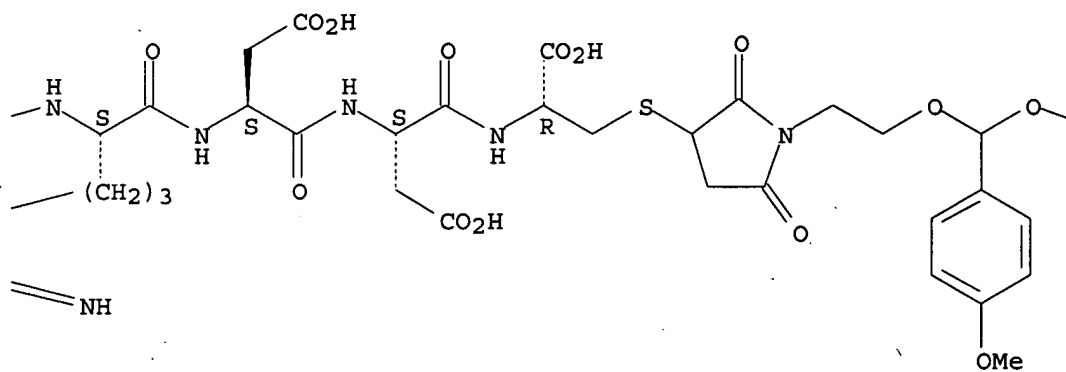
Absolute stereochemistry.

Double bond geometry unknown.

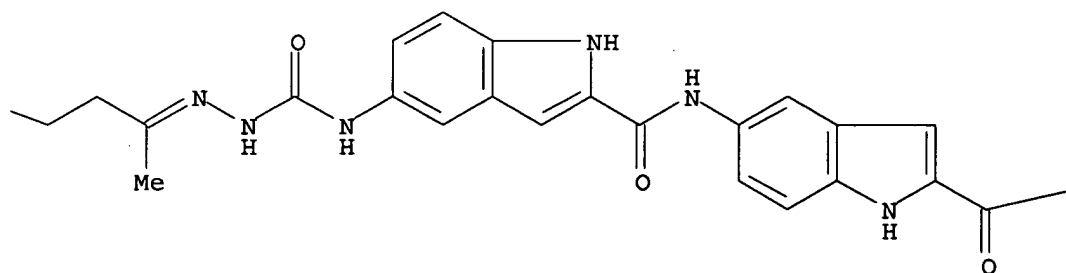
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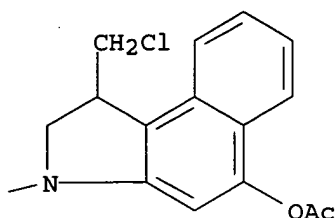
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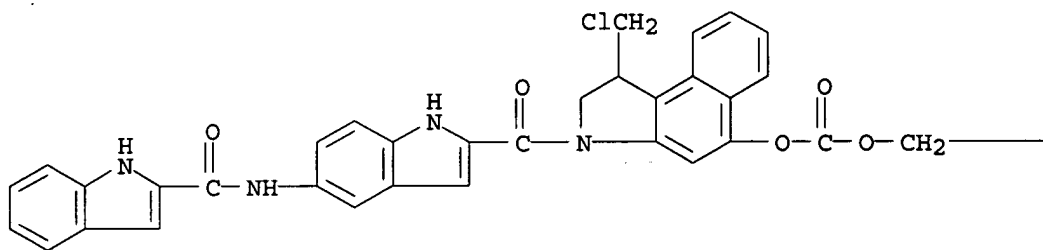
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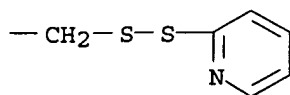
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L26 ANSWER 2 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 742092-08-6 REGISTRY
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 MF C39 H30 Cl N5 O5 S2
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER
 DT.CA Caplus document type: Patent
 RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

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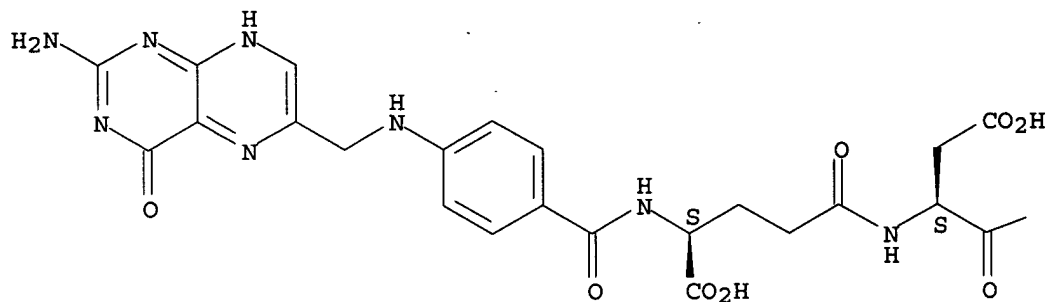
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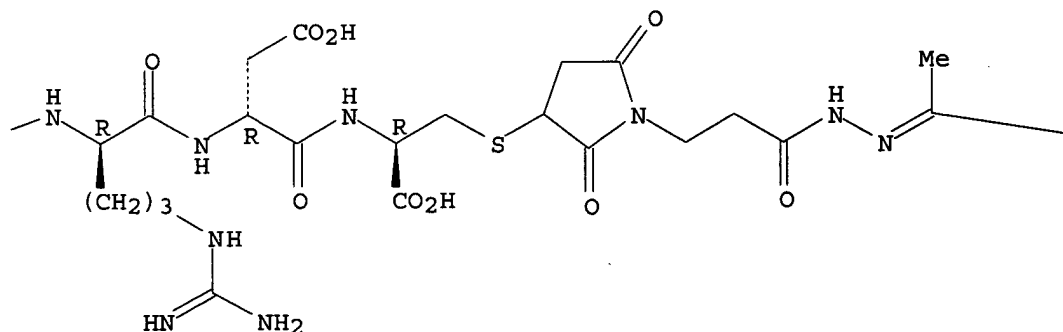
L26 ANSWER 3 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 742092-07-5 REGISTRY
CN INDEX NAME NOT YET ASSIGNED
FS STEREOSEARCH
MF C91 H96 Cl N23 O24 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA Caplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.
Double bond geometry unknown.

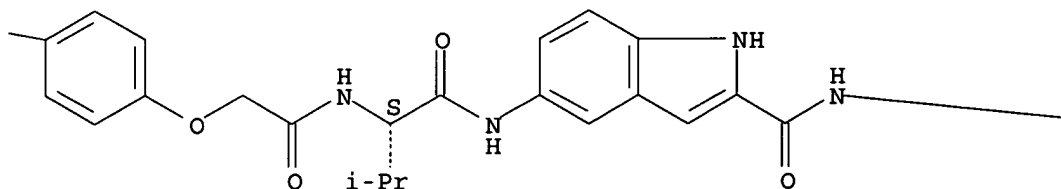
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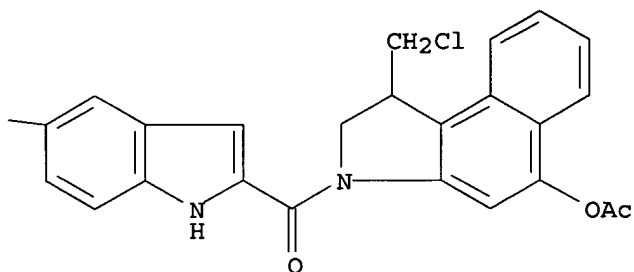
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REFERENCE 1: 141:207525

L26 ANSWER 4 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 742092-06-4 REGISTRY

CN INDEX NAME NOT YET ASSIGNED

FS STEREOSEARCH

MF C76 H77 Cl N22 O21 S

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

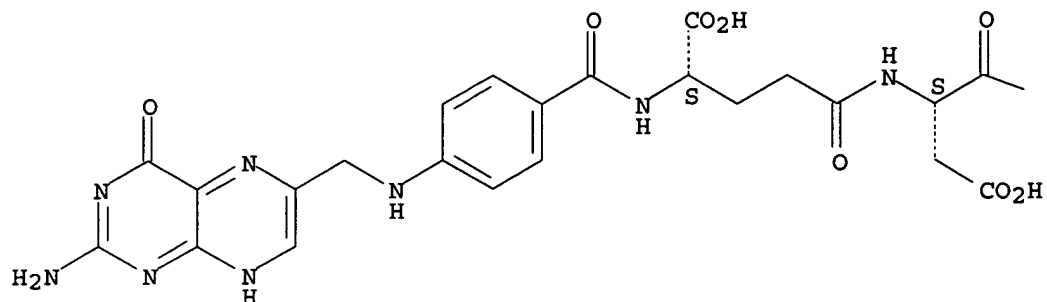
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RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

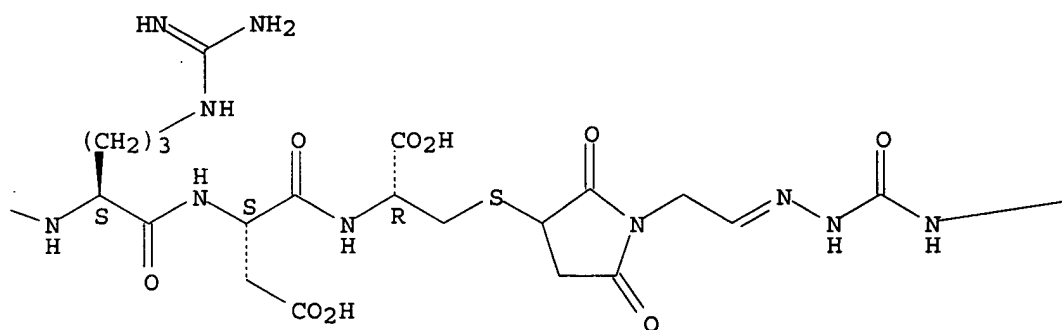
Absolute stereochemistry.

Double bond geometry unknown.

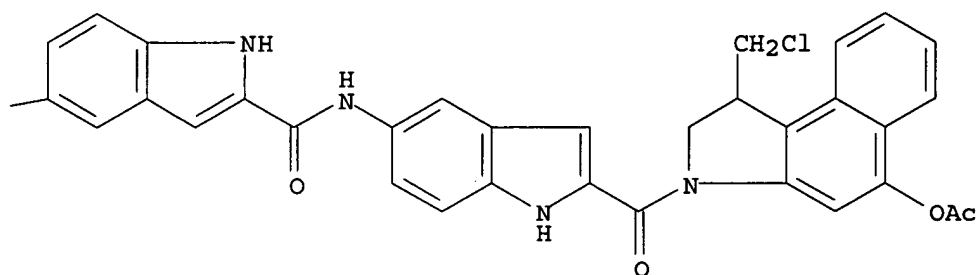
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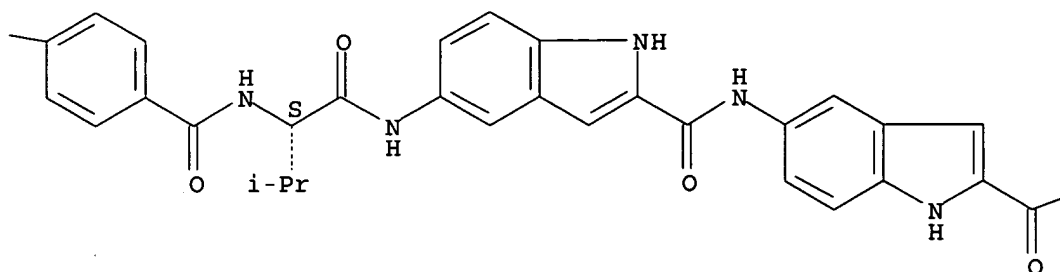
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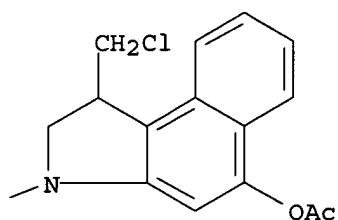
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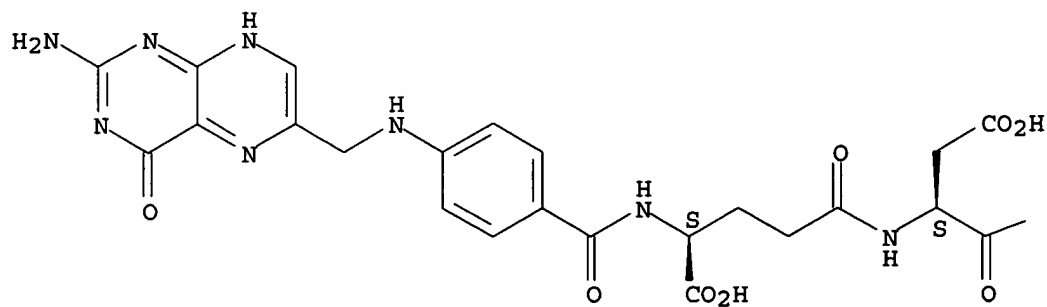
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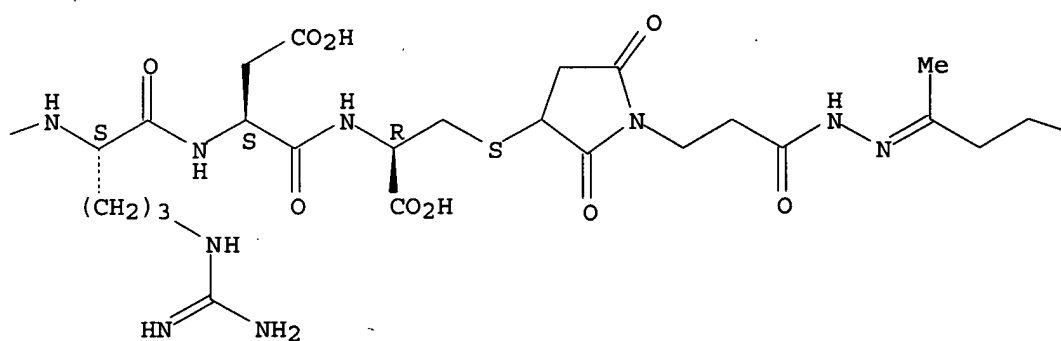
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RN 742092-02-0 REGISTRY
CN INDEX NAME NOT YET ASSIGNED
FS STEREOSEARCH
MF C86 H94 Cl N23 O23 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA Caplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.
Double bond geometry unknown.

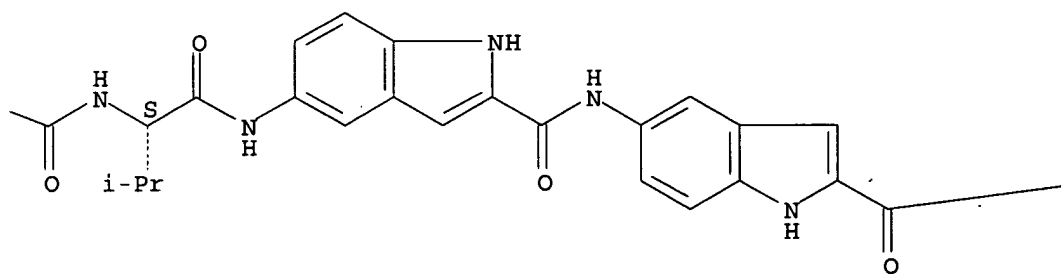
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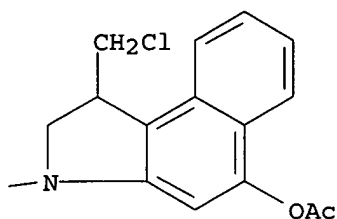
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 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:207525

L26 ANSWER 7 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 742091-92-5 REGISTRY

CN L-Alanine, N-[4-[[[(2-amino-1,4-dihydro-4-oxo-6-pteridiny]methyl)amino]benzoyl]-L-γ-glutamyl-3-[[[bis(carboxymethyl)amino]acetyl]amino]alanyl-3-[[3-[[2-[[[2-[[5-(acetyloxy)-1-(chloromethyl)-1,2-dihydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]amino]-3-oxopropyl]dithio]- (9CI)
 (CA INDEX NAME)

FS STEREOSEARCH

MF C65 H63 Cl N16 O17 S2

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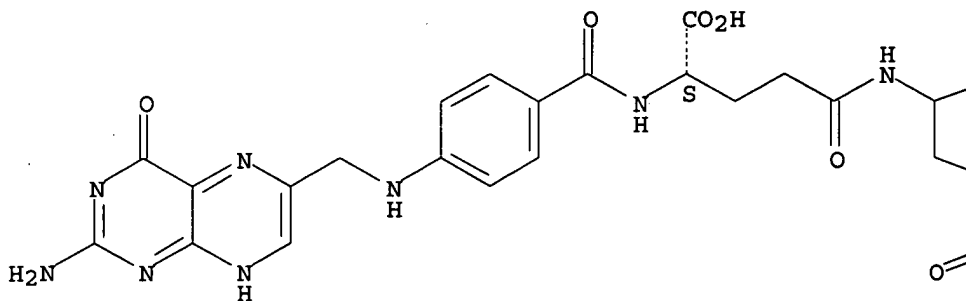
LC STN Files: CA, CAPLUS, TOXCENTER

DT.CA Caplus document type: Patent

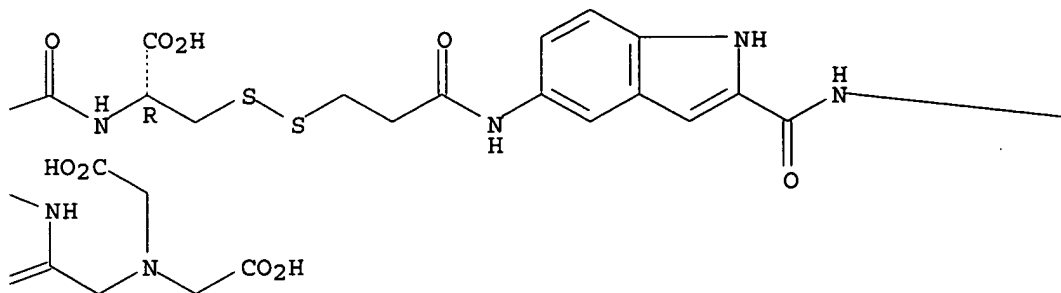
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES
 (Uses)

Absolute stereochemistry.

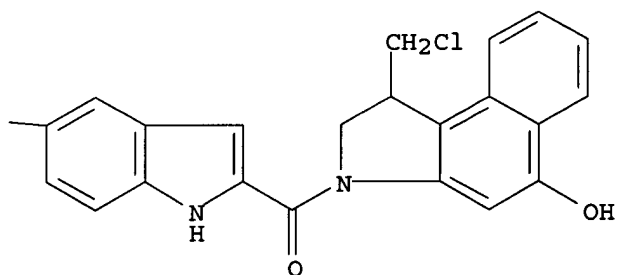
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REFERENCE 1: 141:207525

L26 ANSWER 8 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 742091-91-4 REGISTRY

CN INDEX NAME NOT YET ASSIGNED

FS STEREOSEARCH

MF C76 H86 Cl N19 O18 S2 Si

SR CA

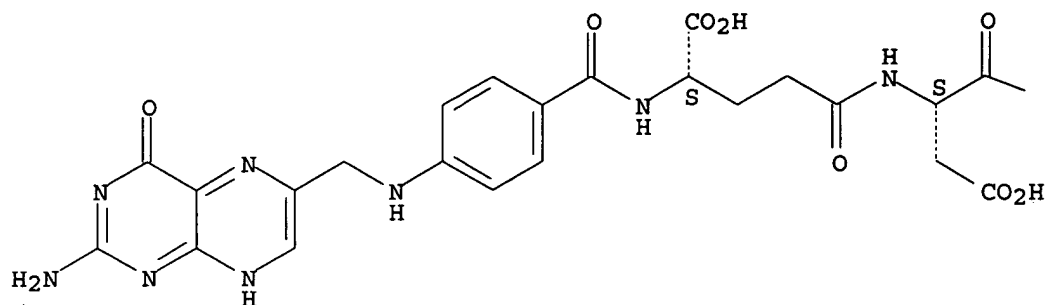
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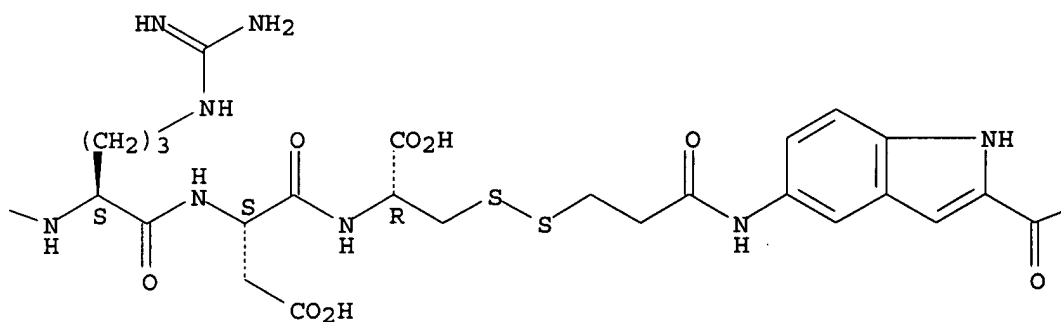
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

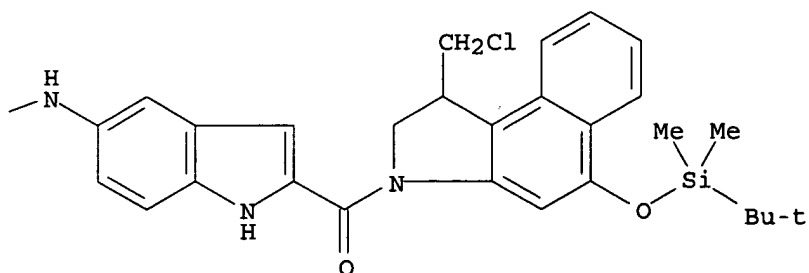
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REFERENCE 1: 141:207525

L26 ANSWER 9 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 742091-89-0 REGISTRY

CN INDEX NAME NOT YET ASSIGNED

FS STEREOSEARCH

MF C72 H74 Cl N19 O19 S2

SR CA

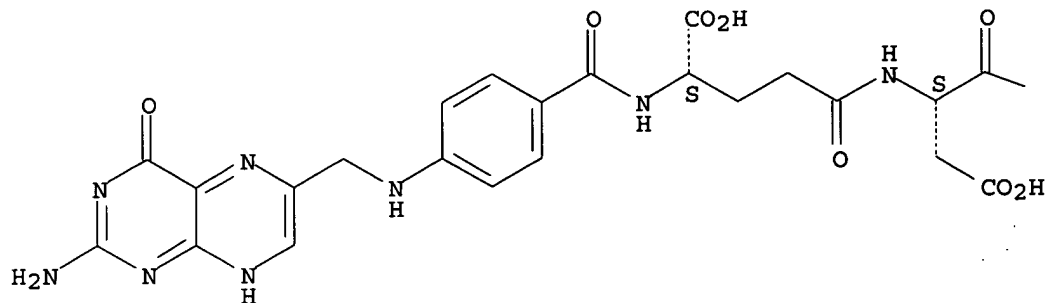
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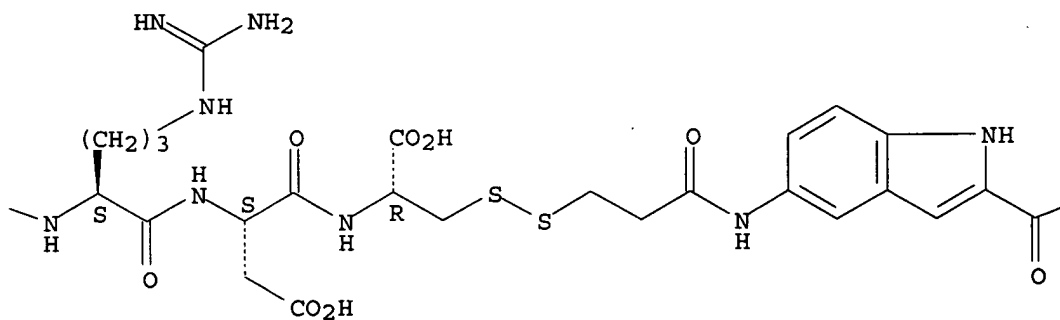
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Absolute stereochemistry.

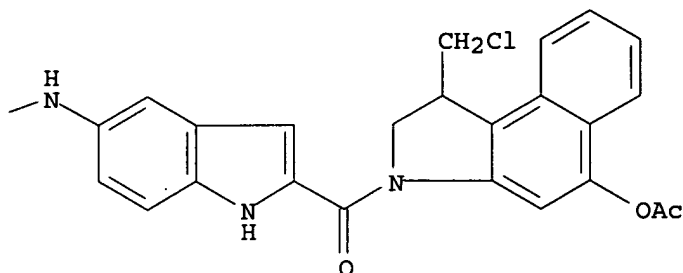
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REFERENCE 1: 141:207525

L26 ANSWER 10 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 742091-88-9 REGISTRY

CN L-Alanine, N-[4-[[[(2-amino-1,4-dihydro-4-oxo-6-pteridiny]methyl)amino]benzoyl]-L-γ-glutamyl-L-arginyl-L-α-aspartyl-3-[[3-[[2-[[[2-[[5-(acetyloxy)-1-(chloromethyl)-1,2-dihydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]amino]-3-oxopropyl]dithio]- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

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SR CA

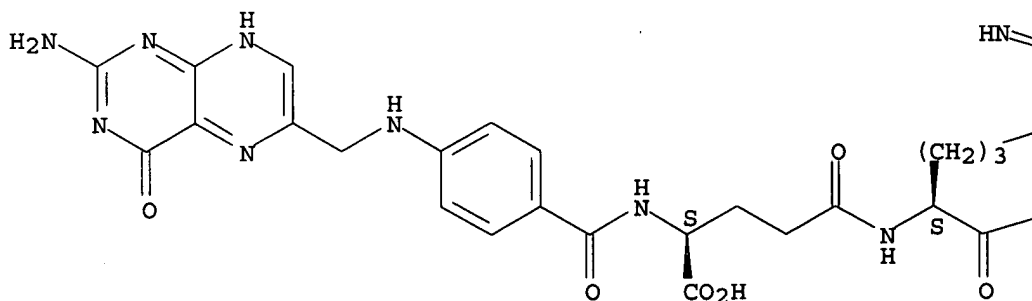
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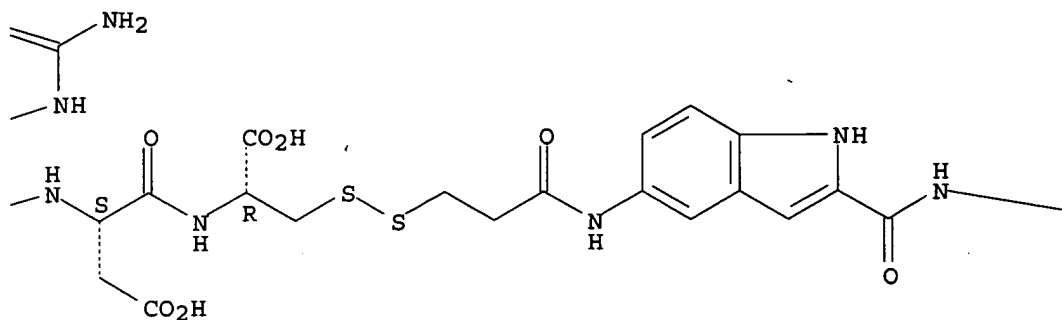
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Absolute stereochemistry.

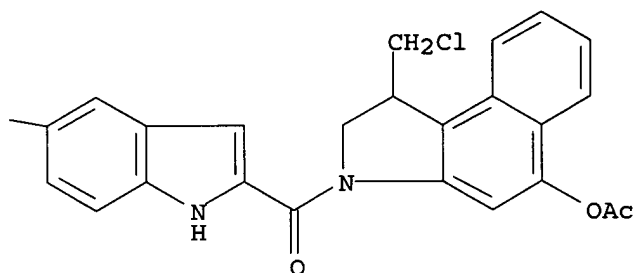
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L26 ANSWER 11 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 742091-87-8 REGISTRY

CN INDEX NAME NOT YET ASSIGNED

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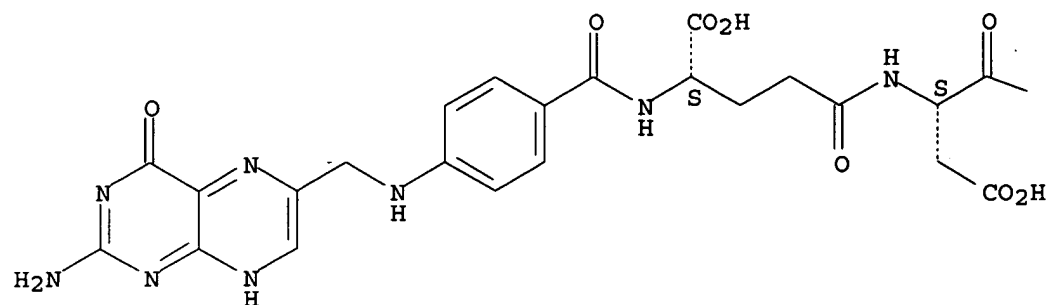
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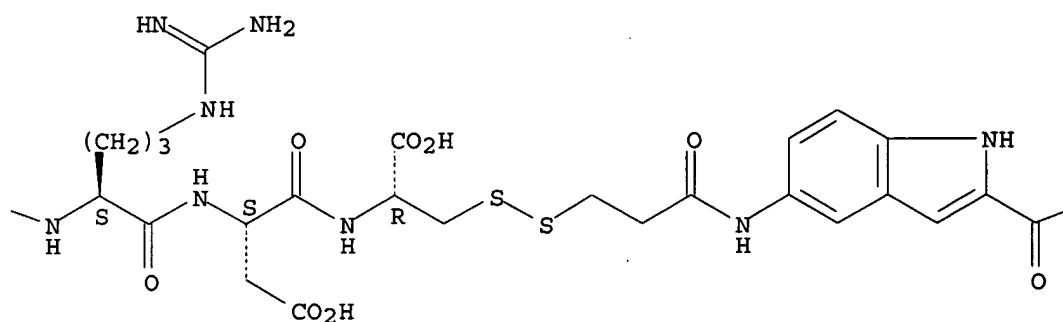
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Absolute stereochemistry.

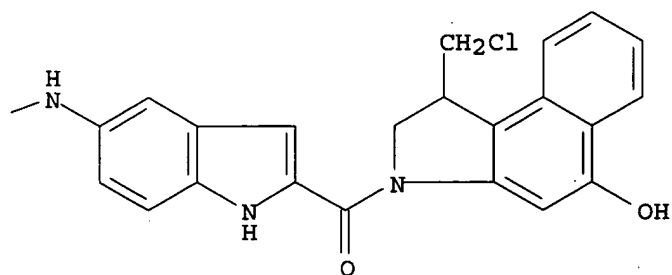
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L26 ANSWER 12 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 742091-86-7 REGISTRY

CN INDEX NAME NOT YET ASSIGNED

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SR CA

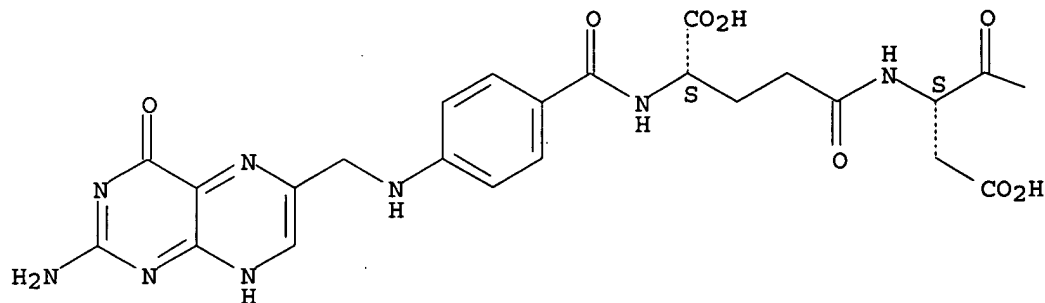
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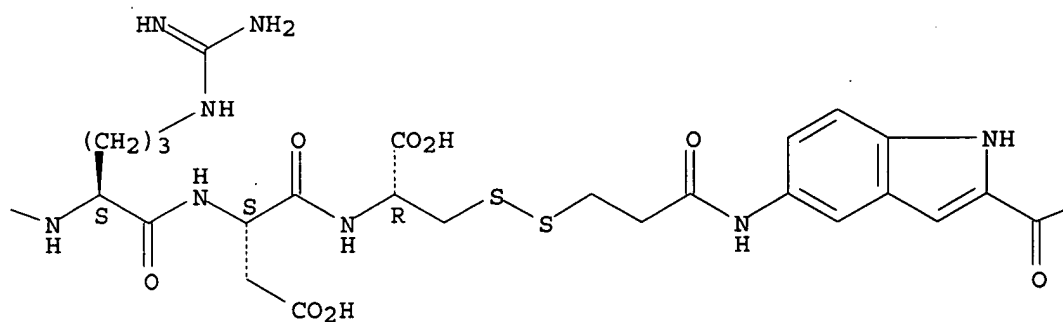
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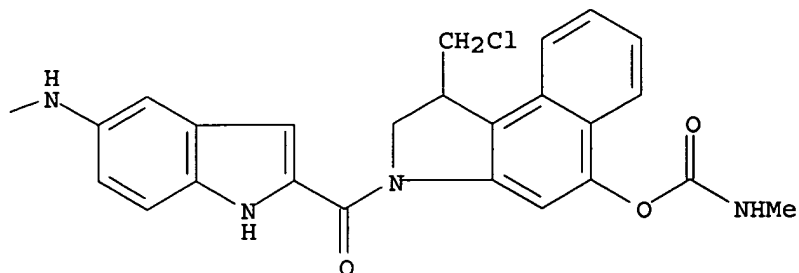
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L26 ANSWER 13 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 742091-83-4 REGISTRY

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FS STEREOSEARCH

MF C66 H67 Cl N18 O15 S2

SR CA

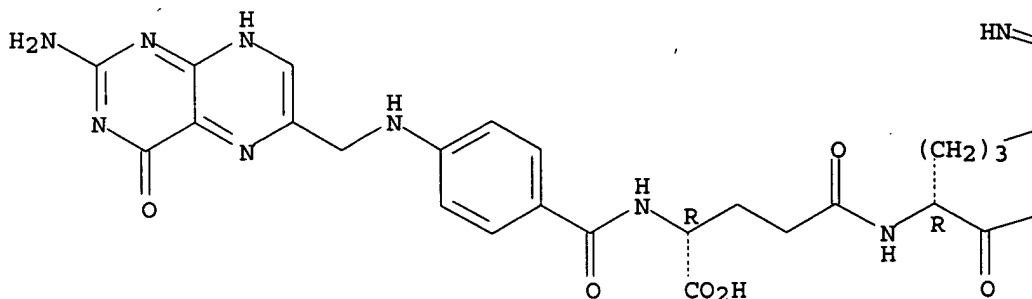
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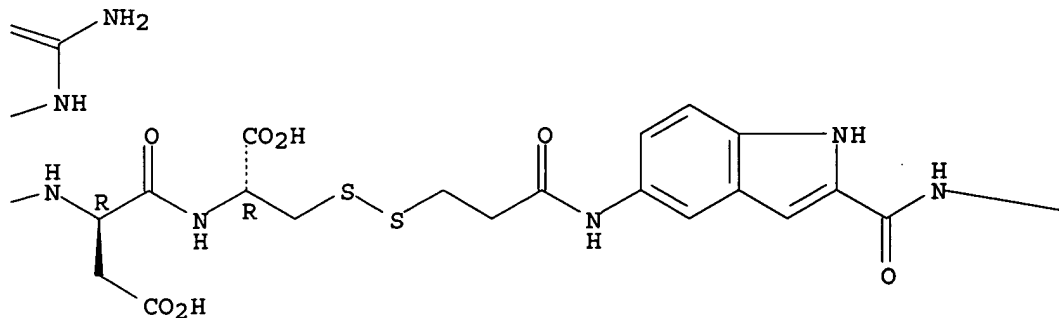
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Absolute stereochemistry.

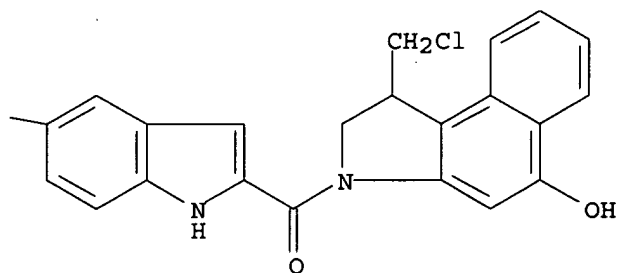
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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:207525

L26 ANSWER 14 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 742091-82-3 REGISTRY

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FS STEREOSEARCH

MF C63 H61 Cl N16 O15 S2

SR CA

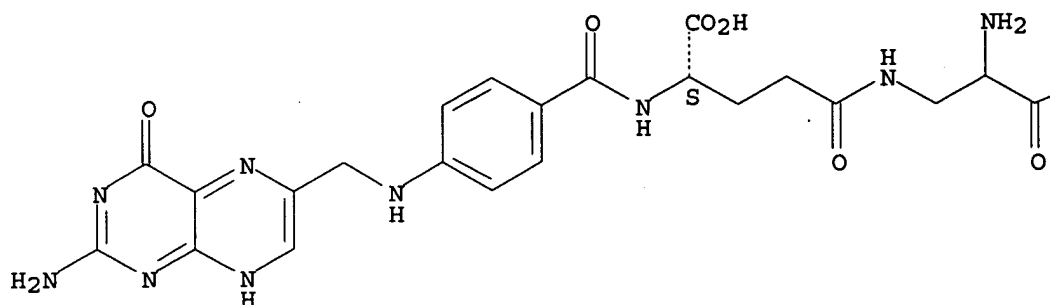
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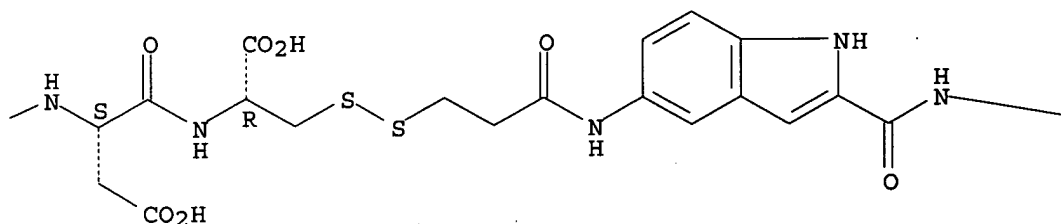
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Absolute stereochemistry.

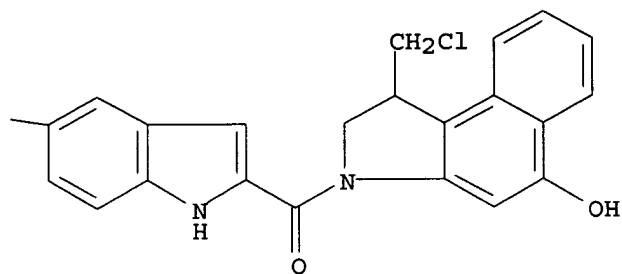
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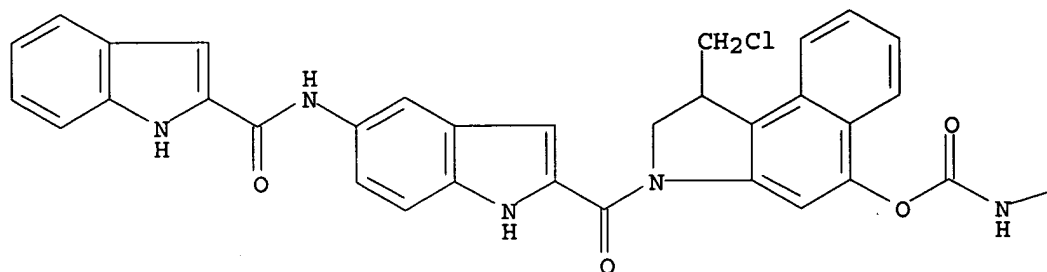
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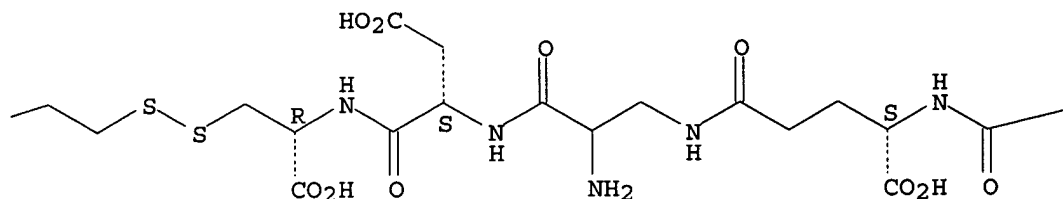
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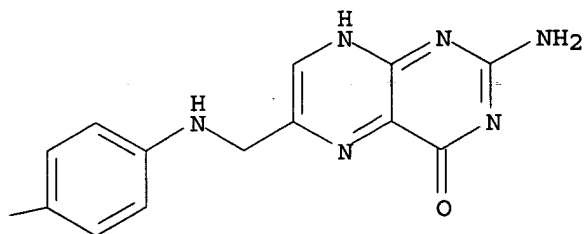
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REFERENCE 1: 141:207525

L26 ANSWER 16 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 742091-68-5 REGISTRY

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FS STEREOSEARCH

MF C66 H63 Cl N14 O18 S2

SR CA

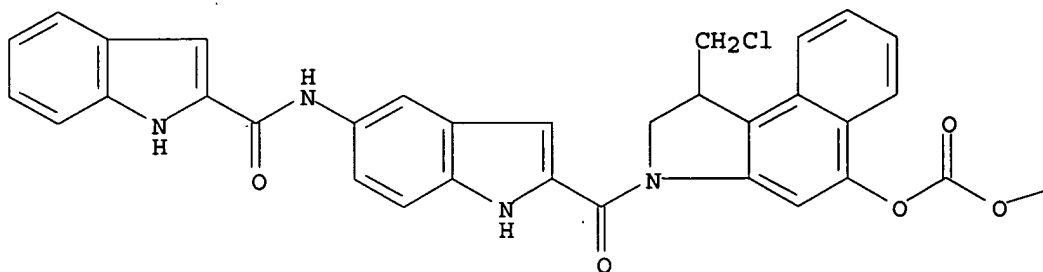
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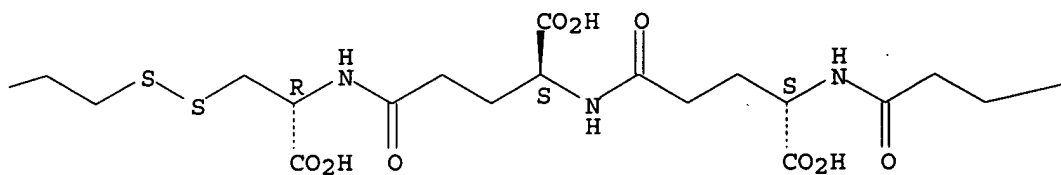
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Absolute stereochemistry.

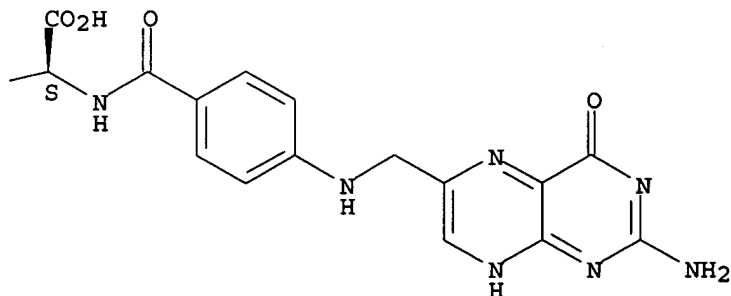
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L26 ANSWER 17 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 742091-66-3 REGISTRY

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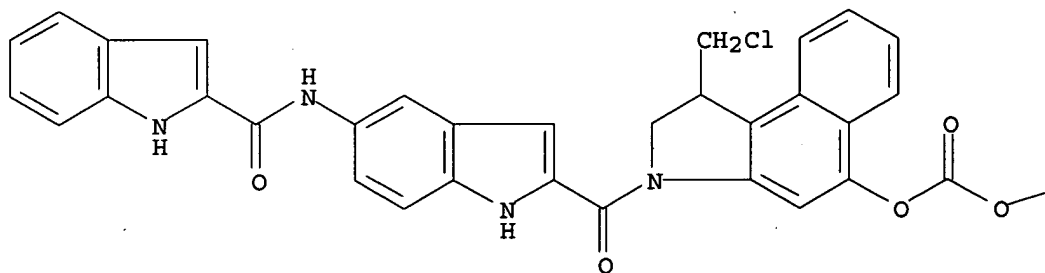
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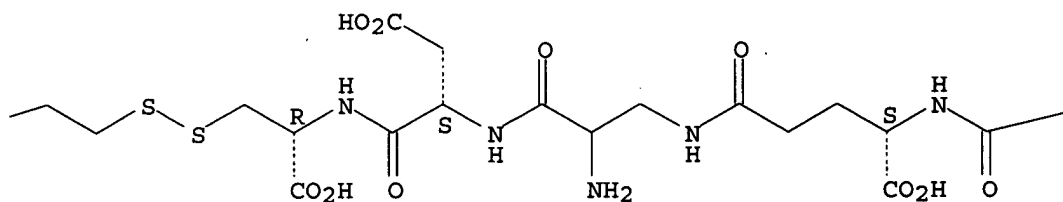
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Absolute stereochemistry.

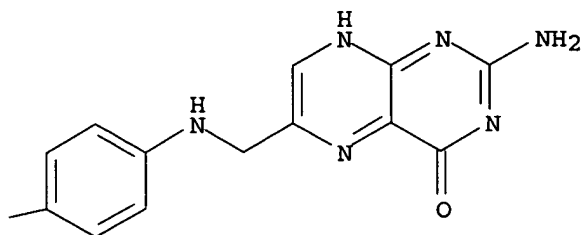
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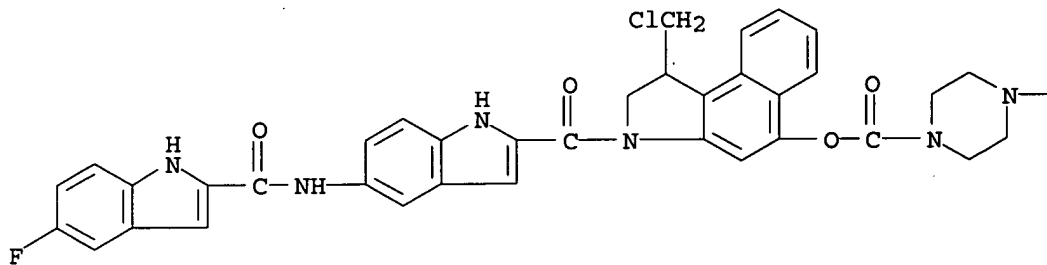
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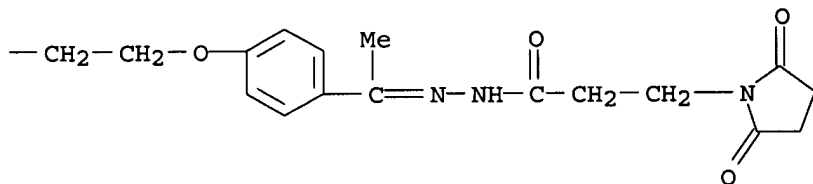
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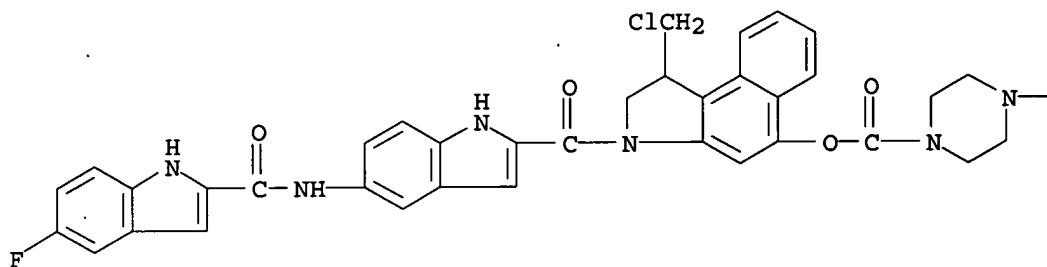
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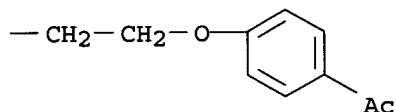
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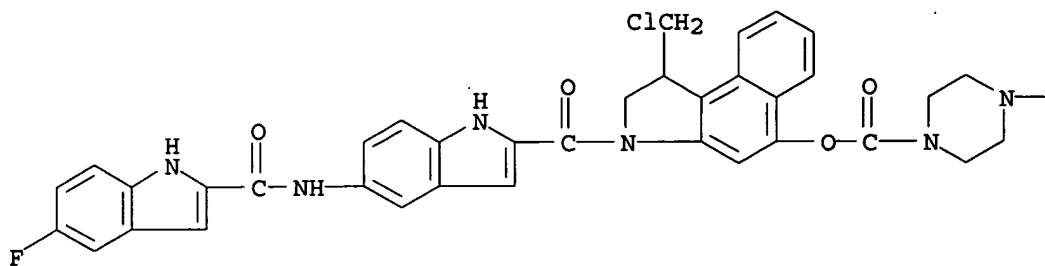
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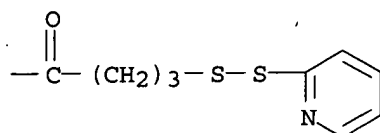
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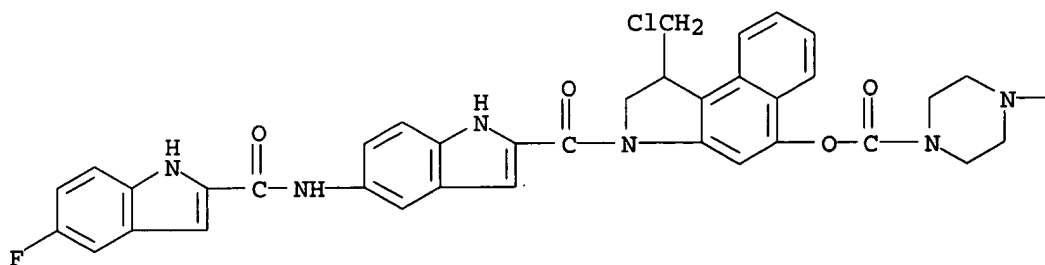
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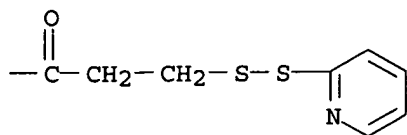
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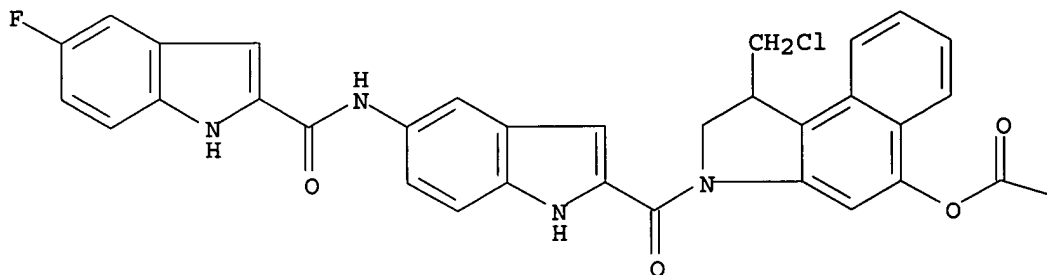
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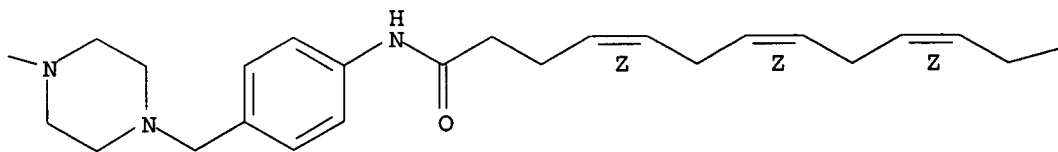
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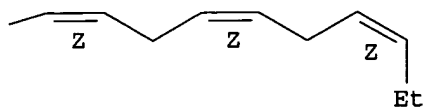
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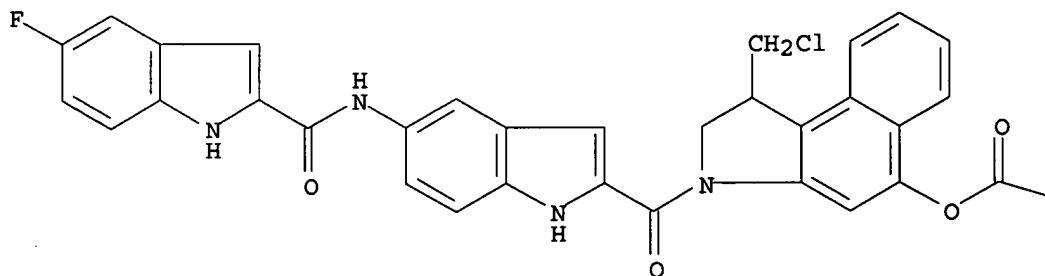
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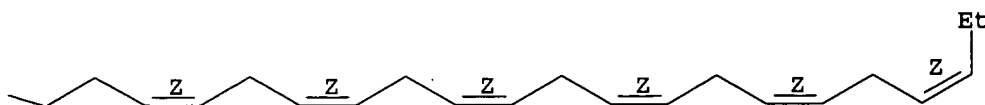
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Double bond geometry as shown.

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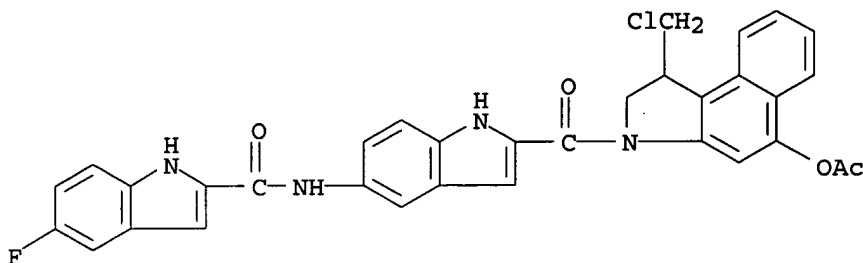
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REFERENCE 1: 141:212819

L26 ANSWER 24 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
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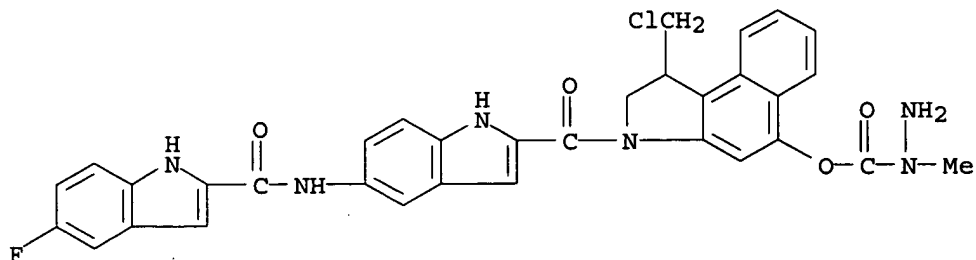


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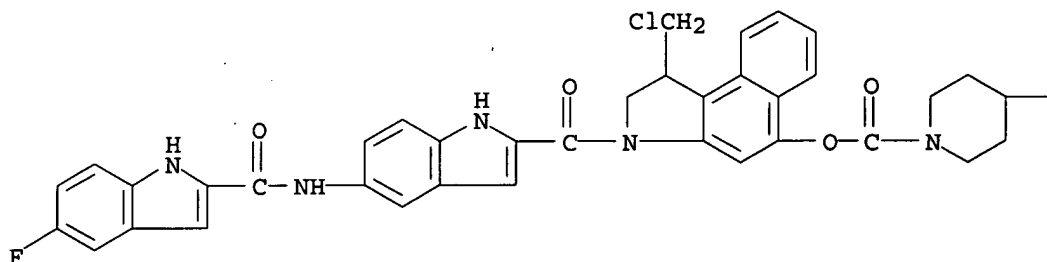
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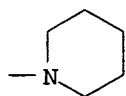
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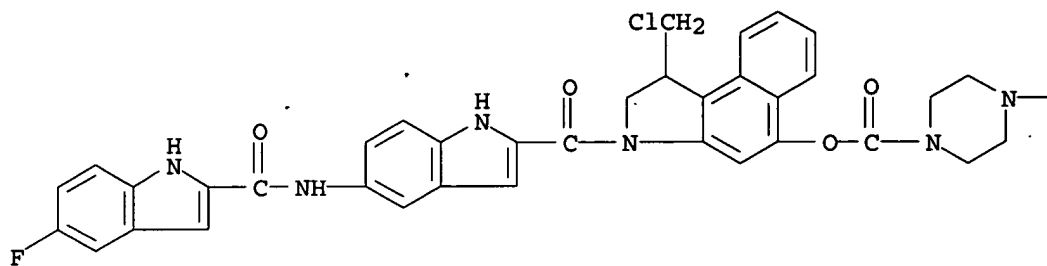
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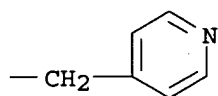
REFERENCE 1: 141:212819

L26 ANSWER 27 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 740841-95-6 REGISTRY
CN INDEX NAME NOT YET ASSIGNED
FS 3D CONCORD
MF C42 H35 Cl F N7 O4
SR CA
LC STN Files: CA, CAPLUS
DT.CA Caplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)

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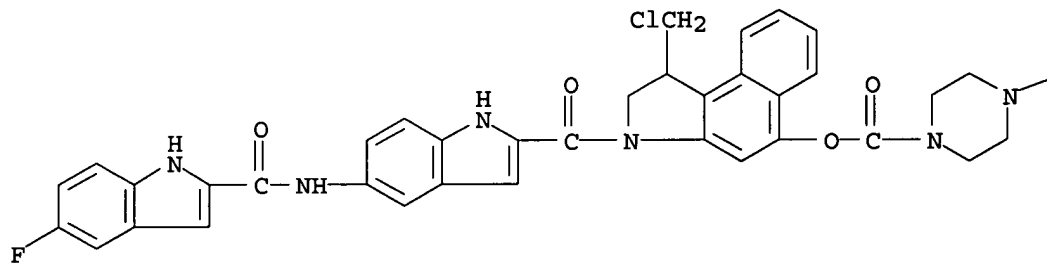
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1 REFERENCES IN FILE CA (1907 TO DATE)
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REFERENCE 1: 141:212819

L26 ANSWER 28 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 740841-94-5 REGISTRY
 CN INDEX NAME NOT YET ASSIGNED
 FS 3D CONCORD
 MF C37 H32 Cl F N6 O4
 SR CA
 LC STN Files: CA, CAPLUS
 DT.CA Caplus document type: Patent
 RL.P Roles from patents: BIOL (Biological study); USES (Uses)

PAGE 1-A



PAGE 1-B

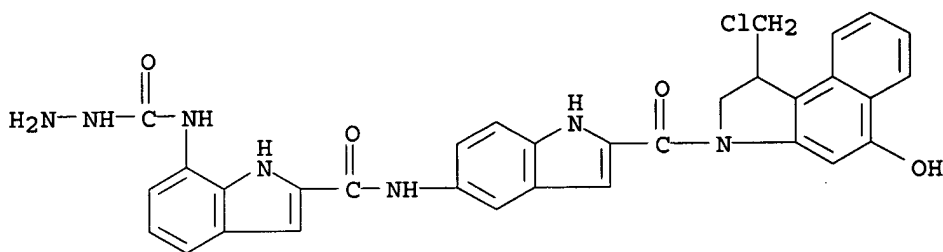


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:212819

L26 ANSWER 29 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 740841-91-2 REGISTRY
CN INDEX NAME NOT YET ASSIGNED
FS 3D CONCORD
MF C32 H26 Cl N7 O4
SR CA
LC STN Files: CA, CAPLUS
DT.CA Caplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

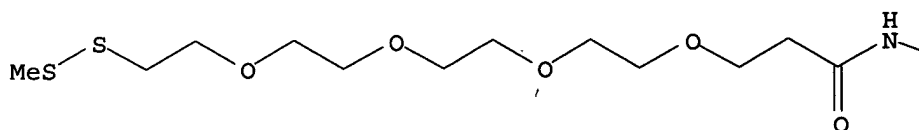
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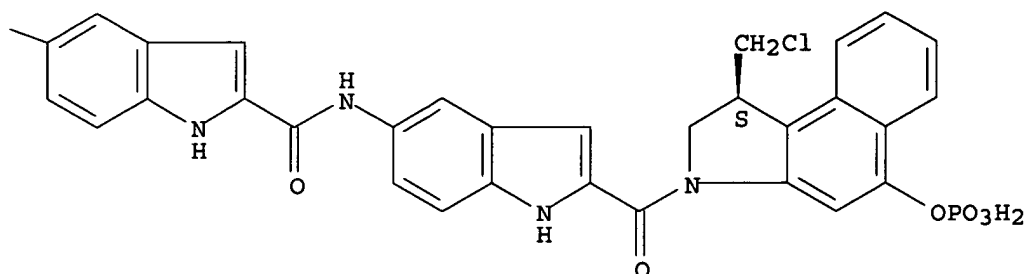
L26 ANSWER 30 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615538-59-5 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-(phosphonooxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[(1-oxo-4,7,10,13-tetraoxa-16,17-dithiaoctadec-1-yl)amino]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C43 H47 Cl N5 O11 P S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA Caplus document type: Patent
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:341741

L26 ANSWER 31 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 615538-58-4 REGISTRY

CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-(phosphonooxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[(1S-mercapto-1-oxo-4,7,10,13-tetraoxapentadec-1-yl)amino]- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C42 H45 Cl N5 O11 P S

SR CA

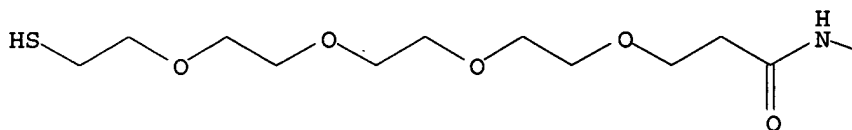
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

DT.CA Caplus document type: Patent

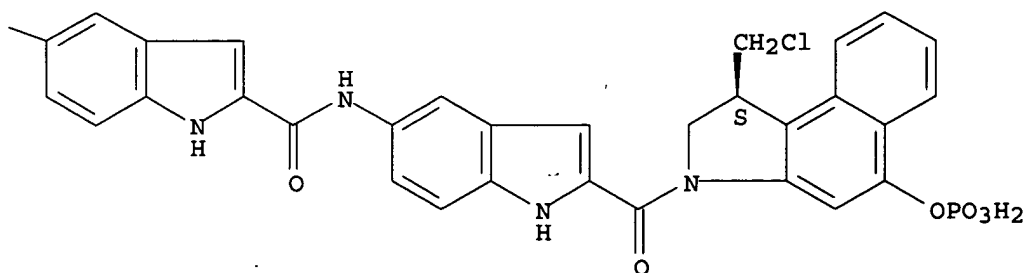
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

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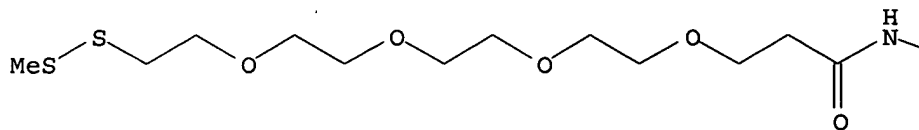
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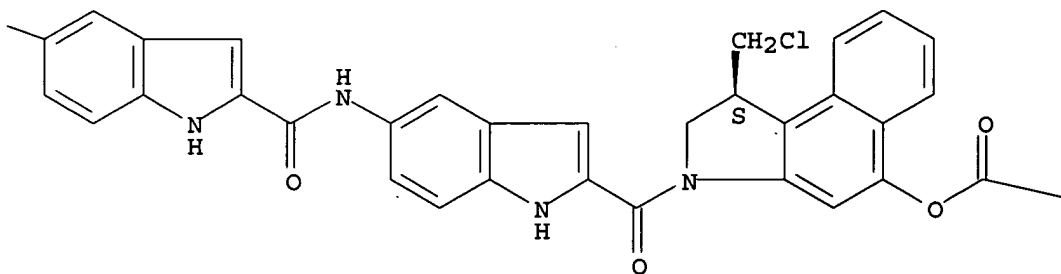
L26 ANSWER 32 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615538-57-3 REGISTRY
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (1S)-1-(chloromethyl)-2,3-dihydro-
3-[[[5-[[[5-[(1-oxo-4,7,10,13-tetraoxa-16,17-dithiaoctadec-1-yl)amino]-1H-
indol-2-yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl
ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C54 H64 Cl N7 O9 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA Caplus document type: Patent
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological
study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

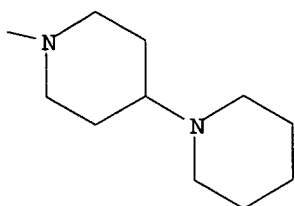
PAGE 1-A



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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:341741

L26 ANSWER 33 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 615538-56-2 REGISTRY

[1,4'-Bipiperidine]-1'-carboxylic acid, (1S)-1-(chloromethyl)-2,3-dihydro-
 3-[[5-[[[5-[(1S-mercapto-1-oxo-4,7,10,13-tetraoxapentadec-1-yl)amino]-1H-
 indol-2-yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl
 ester (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C53 H62 C1 N7 O9 S

SR CA

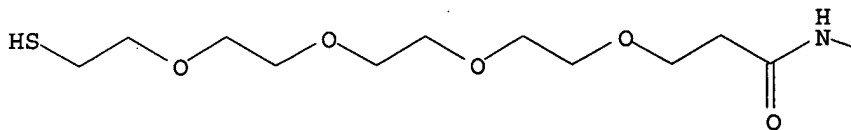
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

DT.CA CAplus document type: Patent

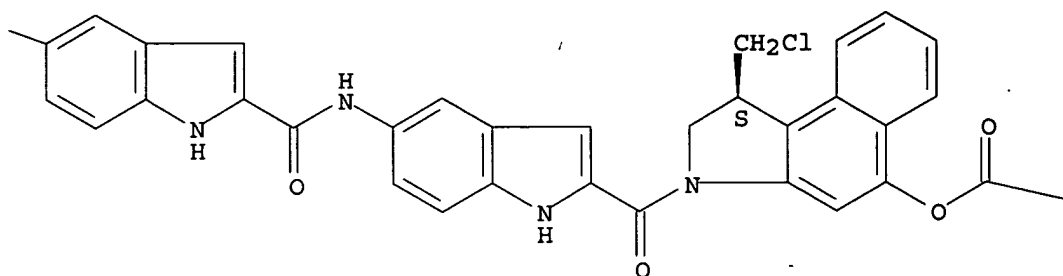
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

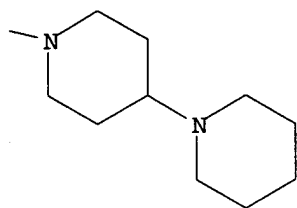
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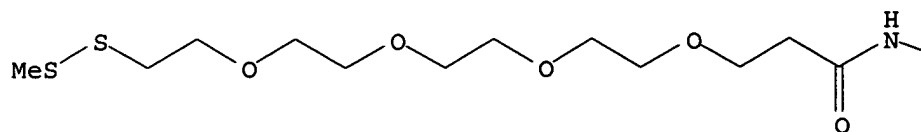
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REFERENCE 1: 139:341741

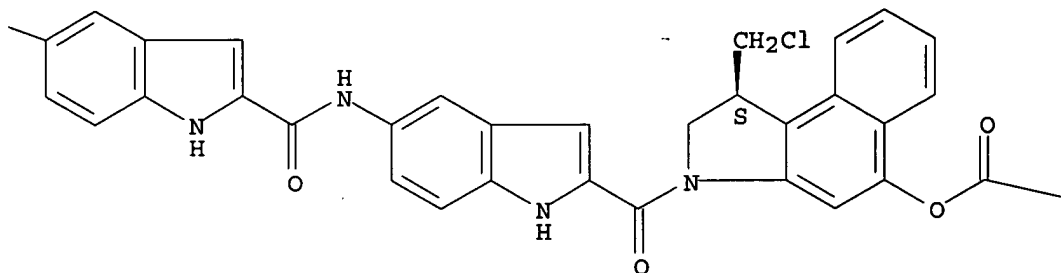
L26 ANSWER 34 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615538-55-1 REGISTRY
CN 1-Piperazinecarboxylic acid, 4-methyl-, (1S)-1-(chloromethyl)-2,3-dihydro-3-[[5-[[[5-[(1-oxo-4,7,10,13-tetraoxa-16,17-dithiaoctadec-1-yl)amino]-1H-indol-2-yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C49 H56 Cl N7 O9 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA Caplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

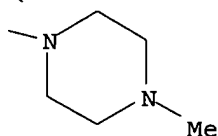
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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:341741

L26 ANSWER 35 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 615538-54-0 REGISTRY

CN 1-Piperazinecarboxylic acid, 4-methyl-, (1S)-1-(chloromethyl)-2,3-dihydro-3-[[[5-[[[5-[(15-mercapto-1-oxo-4,7,10,13-tetraoxapentadec-1-yl)amino]-1H-indol-2-yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl ester (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C48 H54 Cl N7 O9 S

SR CA

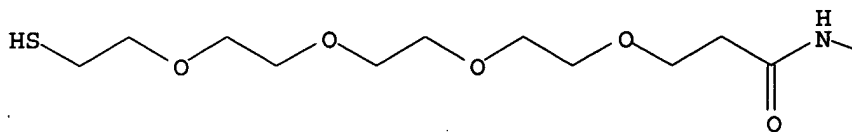
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

DT.CA Caplus document type: Patent

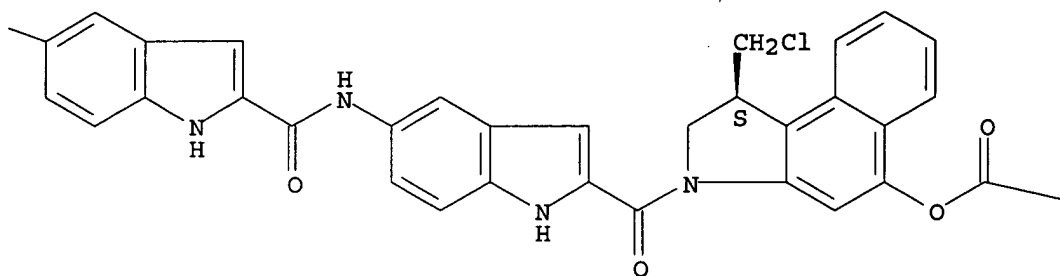
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

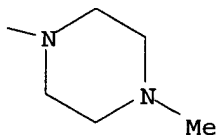
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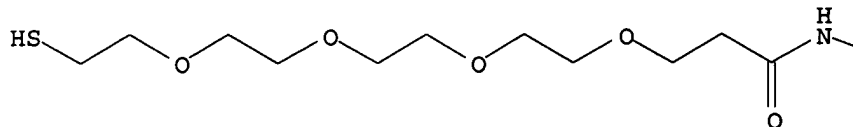
REFERENCE 1: 139:341741

L26 ANSWER 36 OF 89 REGISTRY .COPYRIGHT 2004 ACS on STN
RN 615538-53-9 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]amino]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C42 H44 Cl N5 O8 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA Caplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES

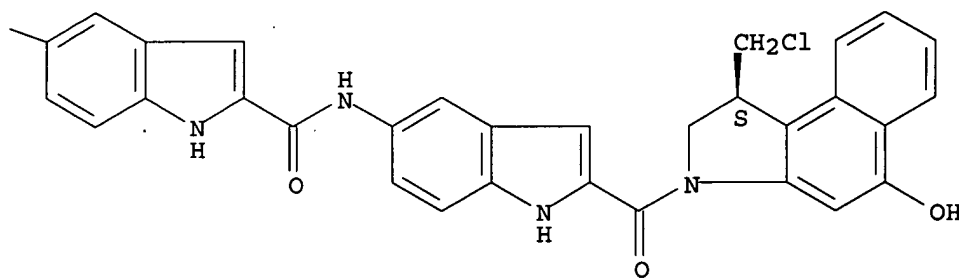
(Uses)

Absolute stereochemistry.

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:341741

L26 ANSWER 37 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 615538-52-8 REGISTRY

CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[(1-oxo-4,7,10,13-tetraoxa-16,17-dithiaoctadec-1-yl)amino]- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C43 H46 Cl N5 O8 S2

SR CA

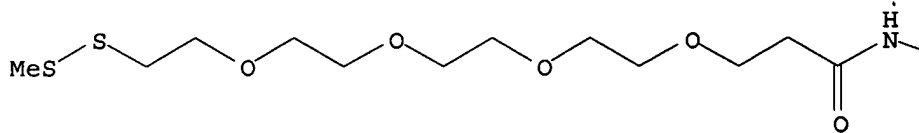
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

DT.CA Caplus document type: Patent

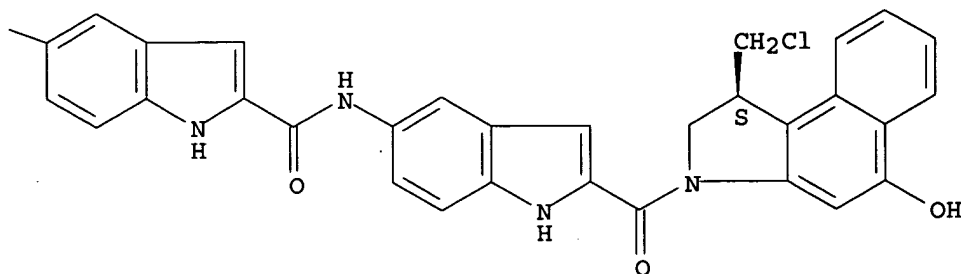
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.

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PAGE 1-B

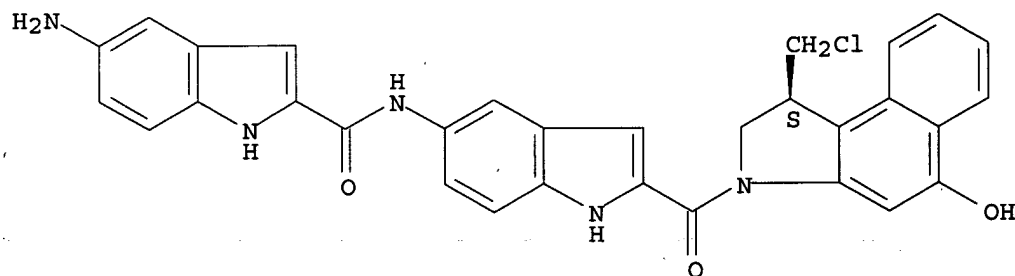


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:341741

L26 ANSWER 38 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615538-51-7 REGISTRY
CN 1H-Indole-2-carboxamide, 5-amino-N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C31 H24 Cl N5 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA Caplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.



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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

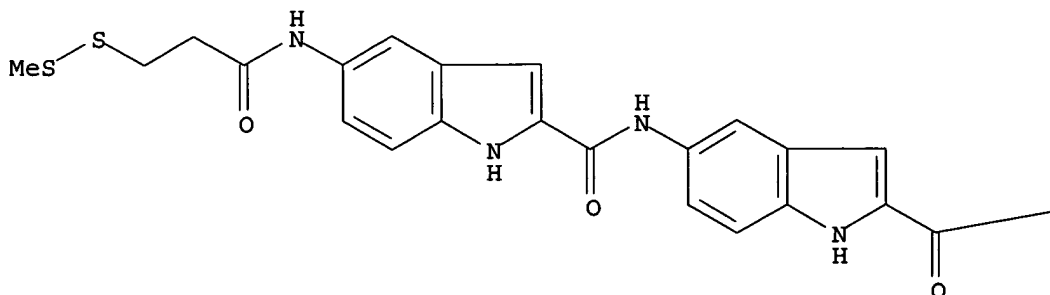
REFERENCE 1: 139:341741

L26 ANSWER 39 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 615538-49-3 REGISTRY
CN Phosphoric acid, (1S)-1-(chloromethyl)-2,3-dihydro-3-[[[5-[[[5-[[3-(methylthio)-1-oxopropyl]amino]-1H-indol-2-yl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl bis(phenylmethyl) ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C49 H43 Cl N5 O7 P S2

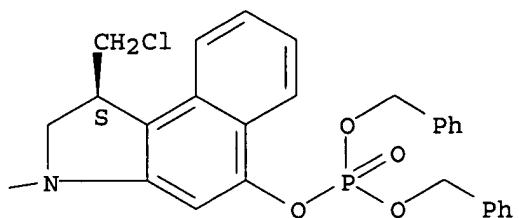
SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
 DT.CA Caplus document type: Patent
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.

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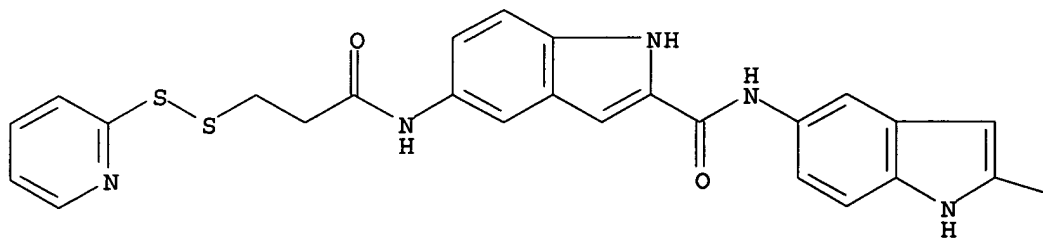
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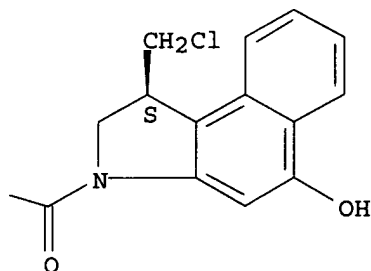
L26 ANSWER 40 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 501666-87-1 REGISTRY
 CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[[1-oxo-3-(2-pyridinyldithio)propyl]amino]]- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C39 H31 Cl N6 O4 S2
 SR CA
 LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL
 DT.CA Caplus document type: Patent
 RL.P Roles from patents: PREP (Preparation)

Absolute stereochemistry.

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 138:238007

L26 ANSWER 41 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 501441-05-0 REGISTRY

CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-nitro- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 1-(S)-Chloromethyl-5-hydroxy-3-[[5-[[[(5-nitroindol-2-yl)carbonyl]amino]indole-2-yl]carbonyl]-1,2-dihydro-3H-benz[e]indole

FS STEREOSEARCH

MF C31 H22 Cl N5 O5

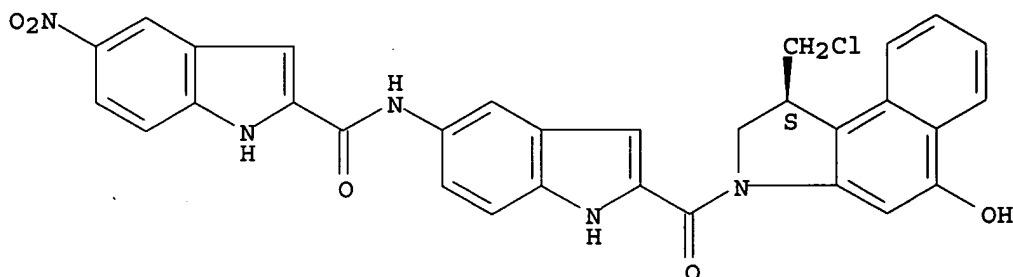
SR CA

LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL

DT.CA Caplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:341741

REFERENCE 2: 138:238007

L26 ANSWER 42 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 500536-51-6 REGISTRY

CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-fluoro- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C31 H22 Cl F N4 O3

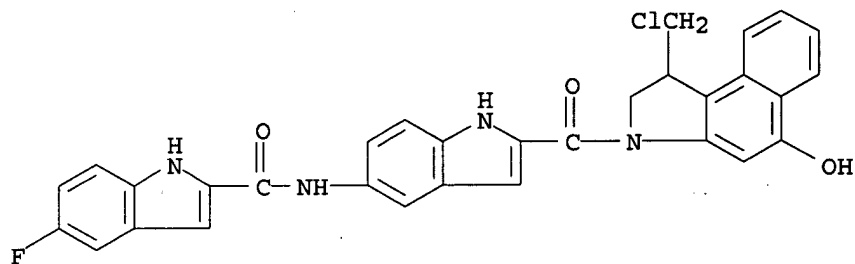
SR CA

LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER

DT.CA Caplus document type: Journal; Patent

RL.P Roles from patents: BIOL (Biological study); USES (Uses)

RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)



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REFERENCE 1: 141:212819

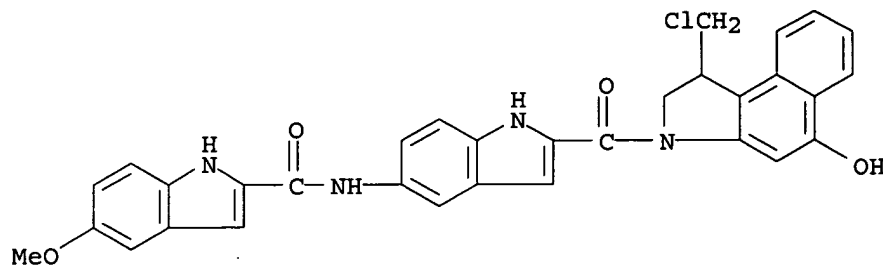
REFERENCE 2: 138:204856

L26 ANSWER 43 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 500536-49-2 REGISTRY

CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-methoxy- (9CI) (CA INDEX NAME)

FS 3D CONCORD
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 DT.CA Caplus document type: Journal; Patent
 RL.P Roles from patents: BIOL (Biological study); USES (Uses)
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)



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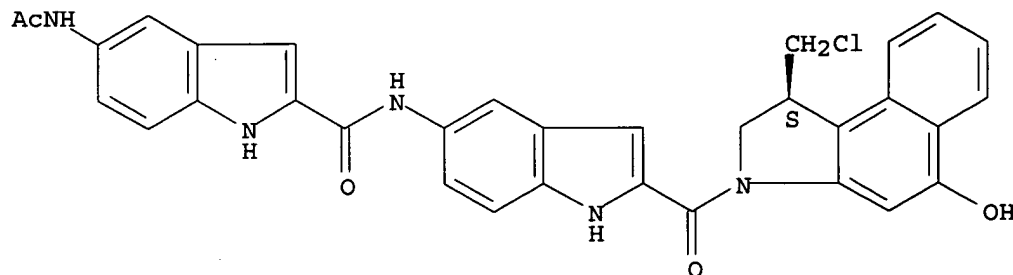
2 REFERENCES IN FILE CA (1907 TO DATE)
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REFERENCE 1: 141:212819

REFERENCE 2: 138:204856

L26 ANSWER 44 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 500536-47-0 REGISTRY
 CN 1H-Indole-2-carboxamide, 5-(acetylamino)-N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]]- (9CI)
 (CA INDEX NAME)
 FS STEREOSEARCH
 MF C33 H26 Cl N5 O4
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER
 DT.CA Caplus document type: Journal
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry. Rotation (+).



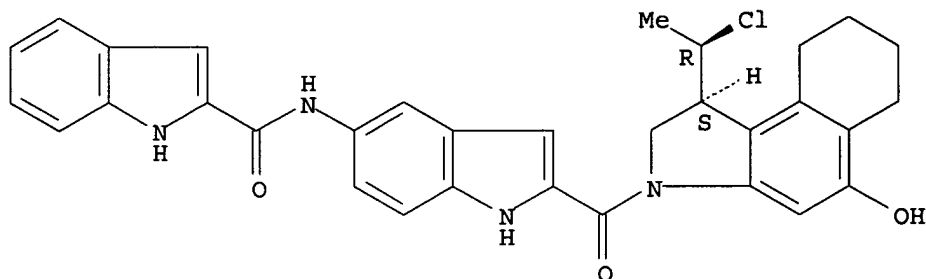
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 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 138:204856

L26 ANSWER 45 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 452921-80-1 REGISTRY

CN 1H-Indole-2-carboxamide, N-[2-[[[(1R)-1-[(1S)-1-chloroethyl]-1,2,6,7,8,9-hexahydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-, rel-(9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C32 H29 Cl N4 O3
 SR CA
 LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
 DT.CA CAPLUS document type: Journal
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Relative stereochemistry.



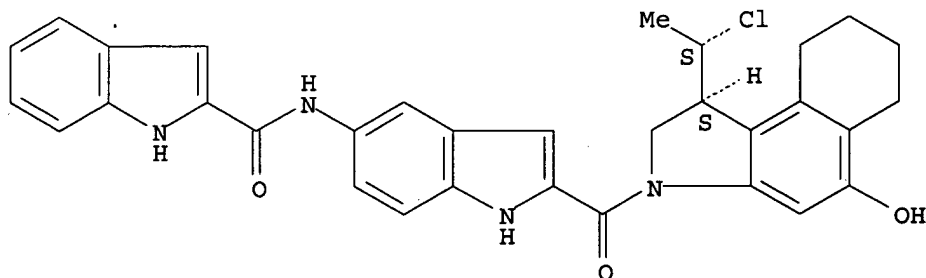
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:201172

L26 ANSWER 46 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 452921-79-8 REGISTRY
 CN 1H-Indole-2-carboxamide, N-[2-[[[(1R)-1-[(1R)-1-chloroethyl]-1,2,6,7,8,9-hexahydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-, rel-(9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C32 H29 Cl N4 O3
 SR CA
 LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
 DT.CA CAPLUS document type: Journal
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Relative stereochemistry.

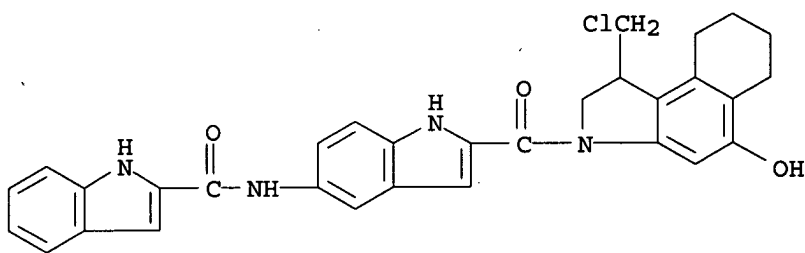


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:201172

L26 ANSWER 47 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 452921-78-7 REGISTRY
 CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2,6,7,8,9-hexahydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C31 H27 Cl N4 O3
 SR CA
 LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
 DT.CA Caplus document type: Journal
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)



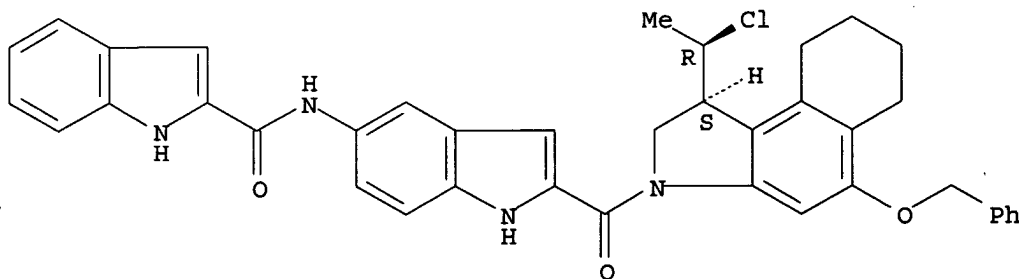
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 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:201172

L26 ANSWER 48 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 452921-77-6 REGISTRY
 CN 1H-Indole-2-carboxamide, N-[2-[[[(1R)-1-[(1S)-1-chloroethyl]-1,2,6,7,8,9-hexahydro-5-(phenylmethoxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-, rel- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C39 H35 Cl N4 O3
 SR CA
 LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
 DT.CA Caplus document type: Journal
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Relative stereochemistry.



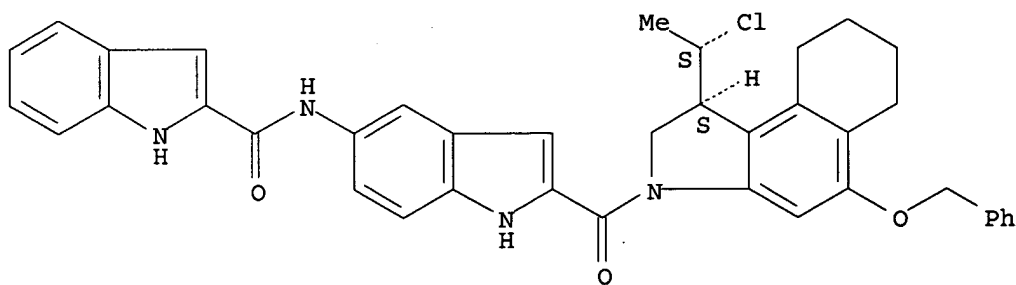
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1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:201172

L26 ANSWER 49 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 452921-76-5 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1R]-1-[(1R)-1-chloroethyl]-1,2,6,7,8,9-hexahydro-5-(phenylmethoxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-, rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C39 H35 Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA Caplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Relative stereochemistry.

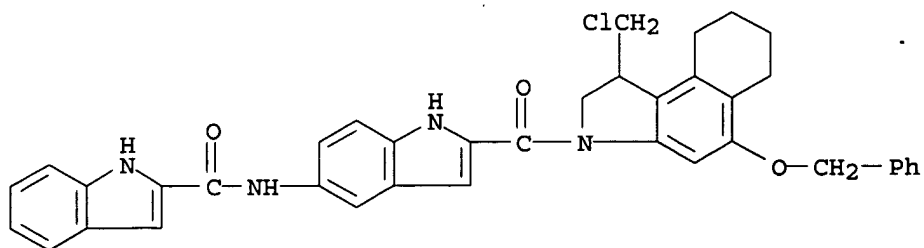


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:201172

L26 ANSWER 50 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 452921-75-4 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2,6,7,8,9-hexahydro-5-(phenylmethoxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C38 H33 Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA Caplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

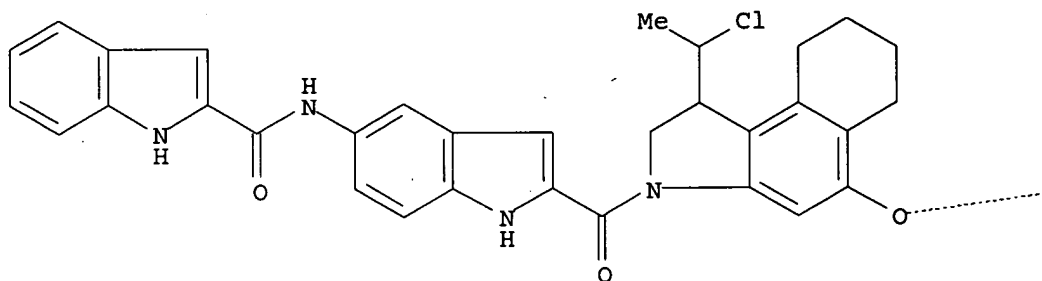
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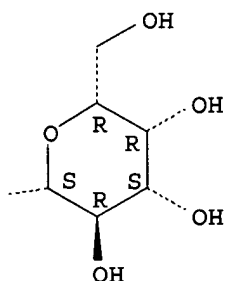
L26 ANSWER 51 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 452921-66-3 REGISTRY
 CN 1H-Indole-2-carboxamide, N-[2-[[1-(1-chloroethyl)-5-(β -D-galactopyranosyloxy)-1,2,6,7,8,9-hexahydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C38 H39 Cl N4 O8
 SR CA
 LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
 DT.CA Caplus document type: Journal
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry.

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

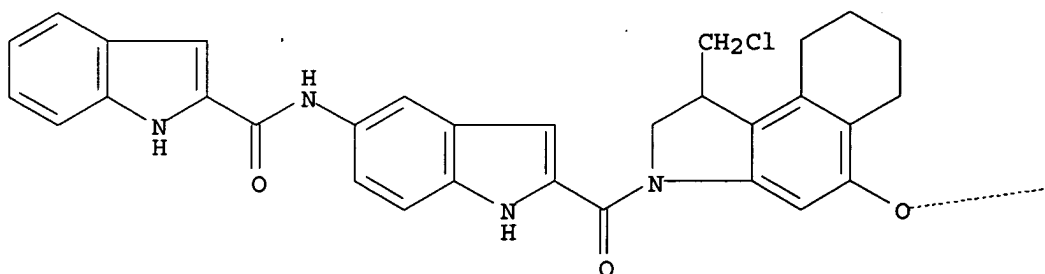
REFERENCE 1: 137:201172

L26 ANSWER 52 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 452921-65-2 REGISTRY
 CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-5-(β -D-galactopyranosyloxy)-1,2,6,7,8,9-hexahydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

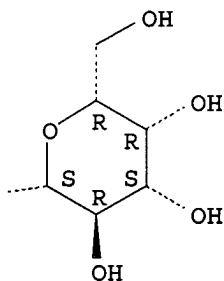
FS STEREOSEARCH
 MF C37 H37 Cl N4 O8
 SR CA
 LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
 DT.CA Caplus document type: Journal
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry.

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PAGE 1-B



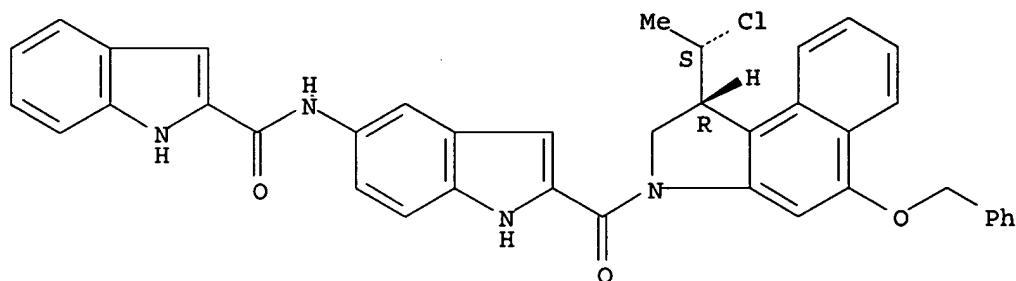
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1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:201172

L26 ANSWER 53 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 390362-73-9 REGISTRY
 CN 1H-Indole-2-carboxamide, N-[2-[[[(1R)-1-[(1S)-1-chloroethyl]-1,2-dihydro-5-(phenylmethoxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C39 H31 Cl N4 O3
 SR CA
 LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
 DT.CA Caplus document type: Journal
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

Absolute stereochemistry.



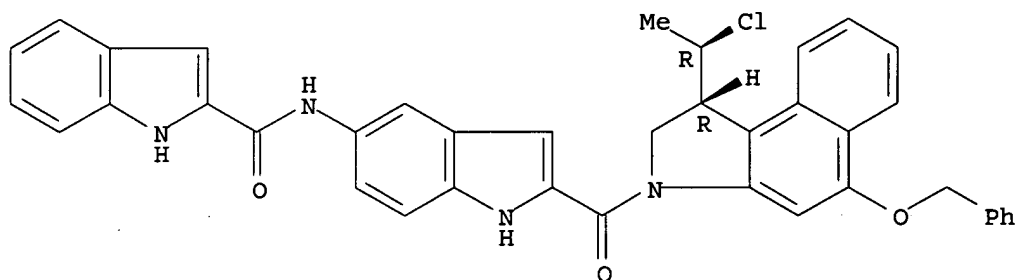
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1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:112208

L26 ANSWER 54 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 390362-72-8 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[[(1R)-1-[(1R)-1-chloroethyl]-1,2-dihydro-5-(phenylmethoxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C39 H31 Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA Caplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

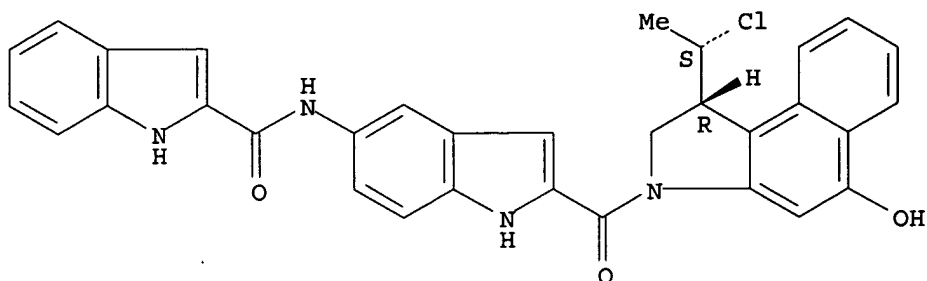
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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:112208

L26 ANSWER 55 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 390362-71-7 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[[(1R)-1-[(1S)-1-chloroethyl]-1,2-dihydro-5-(phenylmethoxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H25 Cl N4 O3

SR CA
 LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
 DT.CA Caplus document type: Journal
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation);
 PRP (Properties); USES (Uses)

Absolute stereochemistry.



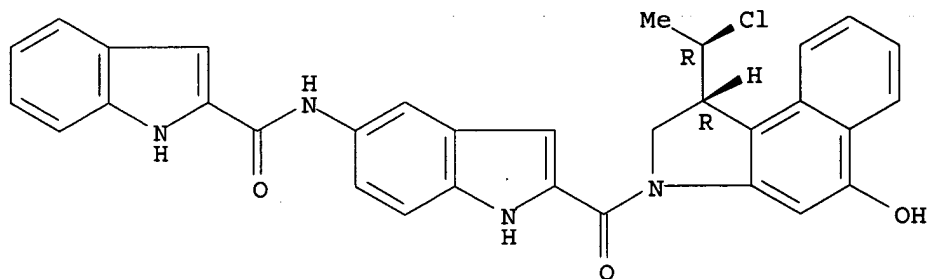
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1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:112208

L26 ANSWER 56 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 390362-70-6 REGISTRY
 CN 1H-Indole-2-carboxamide, N-[2-[[[(1R)-1-[(1R)-1-chloroethyl]-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C32 H25 Cl N4 O3
 SR CA
 LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
 DT.CA Caplus document type: Journal
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation);
 PRP (Properties); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

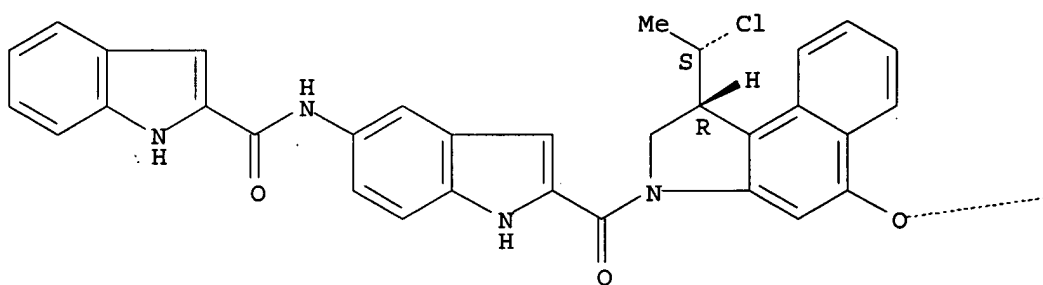
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REFERENCE 1: 136:112208

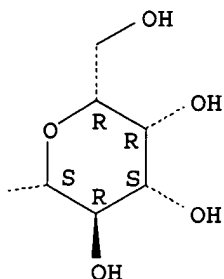
L26 ANSWER 57 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 390362-69-3 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[[(1R)-1-[(1S)-1-chloroethyl]-5-(β-D-galactopyranosyloxy)-1,2-dihydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C38 H35 Cl N4 O8
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA Caplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

Absolute stereochemistry.

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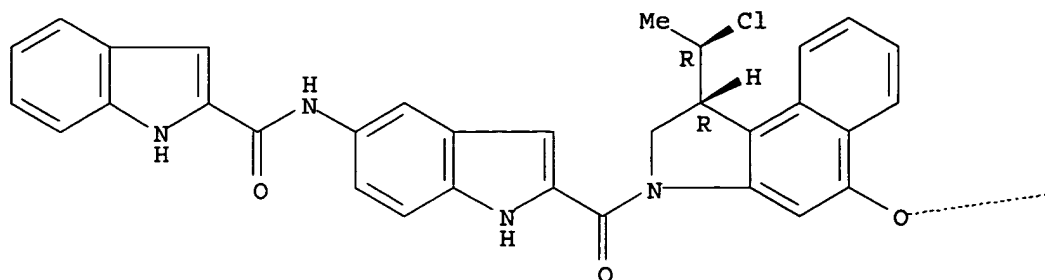
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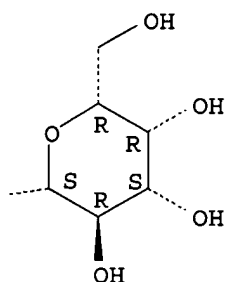
L26 ANSWER 58 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 390362-68-2 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[[(1R)-1-[(1R)-1-chloroethyl]-5-(β-D-galactopyranosyloxy)-1,2-dihydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C38 H35 Cl N4 O8
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA Caplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

Absolute stereochemistry.

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:112208

L26 ANSWER 59 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 390362-64-8 REGISTRY

CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2-dihydro-5-(phenylmethoxy)-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

FS 3D CONCORD

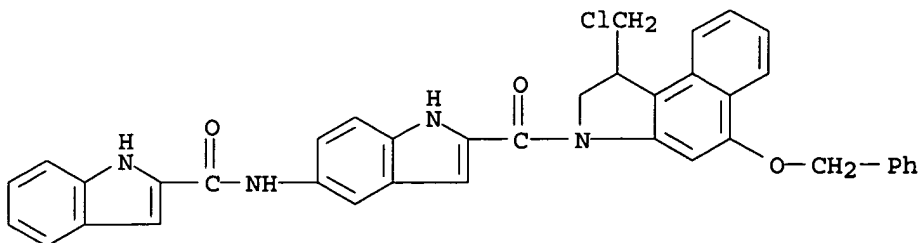
MF C38 H29 Cl N4 O3

SR CA

LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER

DT.CA CAplus document type: Journal

RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

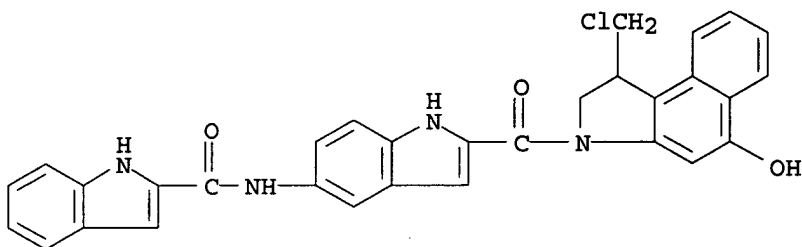


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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REFERENCE 1: 136:112208

L26 ANSWER 60 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 390362-63-7 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C31 H23 Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA Caplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation);
PRP (Properties); USES (Uses)



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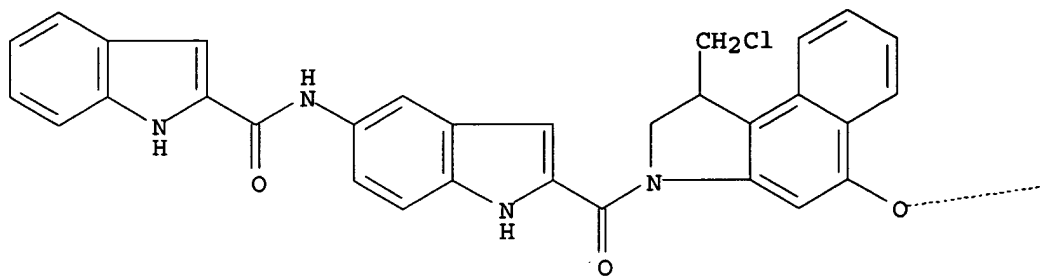
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REFERENCE 1: 136:112208

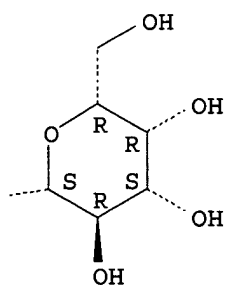
L26 ANSWER 61 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 390362-62-6 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-5-(β-D-galactopyranosyloxy)-1,2-dihydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C37 H33 Cl N4 O8
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA Caplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation);
PRP (Properties); USES (Uses)

Absolute stereochemistry.

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

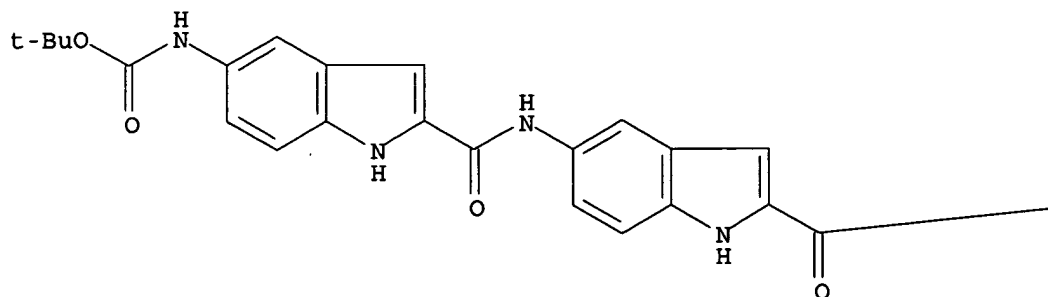
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REFERENCE 1: 136:112208

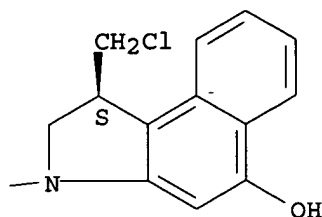
L26 ANSWER 62 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 372954-24-0 REGISTRY
CN Carbamic acid, [2-[[[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C36 H32 Cl N5 O5
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER
DT.CA Caplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry.

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 138:255007

REFERENCE 2: 135:357786

L26 ANSWER 63 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 330206-90-1 REGISTRY

CN 1H-Indole-2-carboxamide, N-[2-[[1-(1-chloroethyl)-5-(β-D-galactopyranosyloxy)-1,2-dihydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C38 H35 Cl N4 O8

SR CA

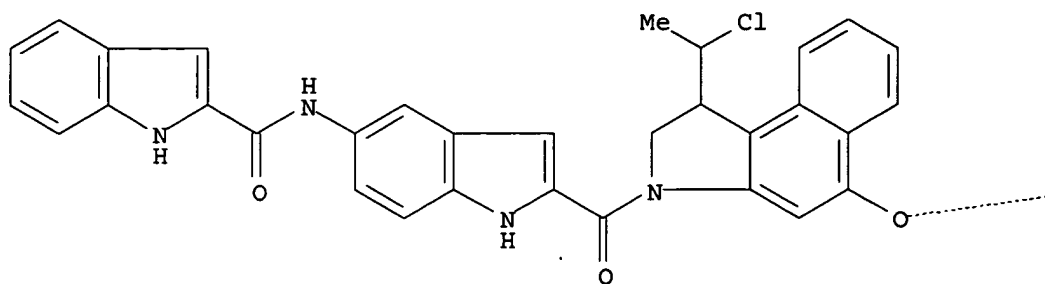
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

DT.CA Caplus document type: Patent

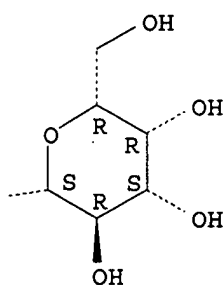
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)

2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 135:344672

REFERENCE 2: 134:237751

L26 ANSWER 64 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 330206-89-8 REGISTRY

CN 1H-Indole-2-carboxamide, N-[2-[[1-(1-chloroethyl)-1,2-dihydro-5-[(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)oxy]-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C46 H43 Cl N4 O12

SR CA

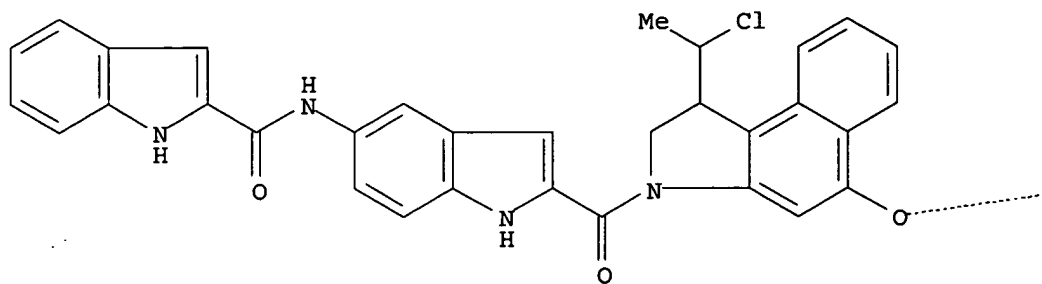
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

DT.CA Caplus document type: Patent

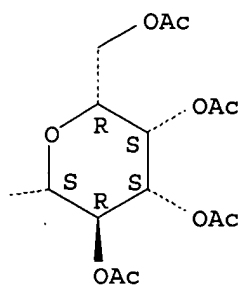
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 135:344672

REFERENCE 2: 134:237751

L26 ANSWER 65 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 244154-68-5 REGISTRY

CN 1H-Indole-2-carboxamide, N-[2-[[[(1R)-1-(chloromethyl)-1,2-dihydro-5-
 [[(phenylamino)carbonyl]oxy]-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-
 (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C38 H28 Cl N5 O4

SR CA

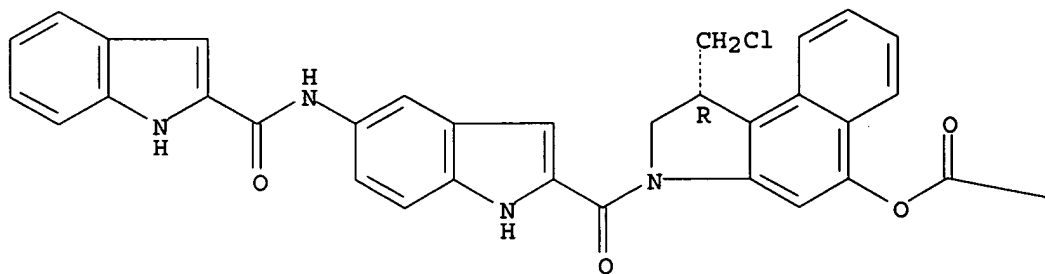
LC STN Files: CA, CAPLUS, TOXCENTER

DT.CA Caplus document type: Journal

RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry. Rotation (-).

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:237670

L26 ANSWER 66 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 244154-65-2 REGISTRY

CN 1-Piperazinebutanoic acid, 4-methyl-γ-oxo-, (1S)-1-(chloromethyl)-
 2,3-dihydro-3-[[5-[(1H-indol-2-ylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-
 1H-benz[e]indol-5-yl ester (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C40 H37 Cl N6 O5

SR CA

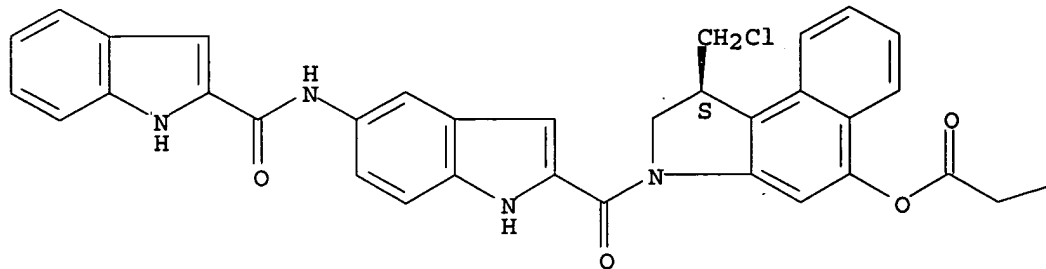
LC STN Files: CA, CAPLUS, TOXCENTER

DT.CA Caplus document type: Journal

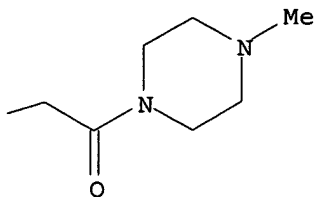
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry. Rotation (+).

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PAGE 1-B



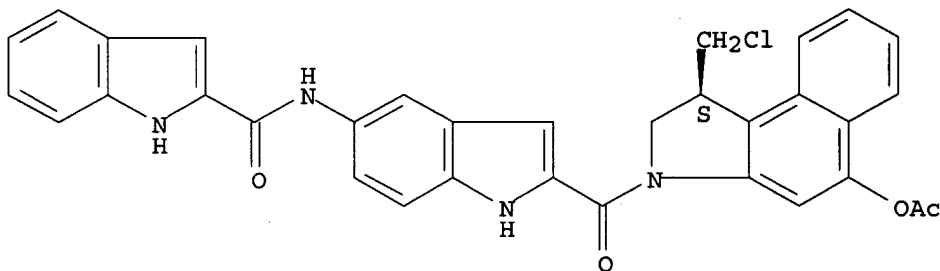
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:237670

L26 ANSWER 67 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 244154-64-1 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-5-(acetyloxy)-1-(chloromethyl)-1,2-dihydro-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C33 H25 Cl N4 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAPLUS document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

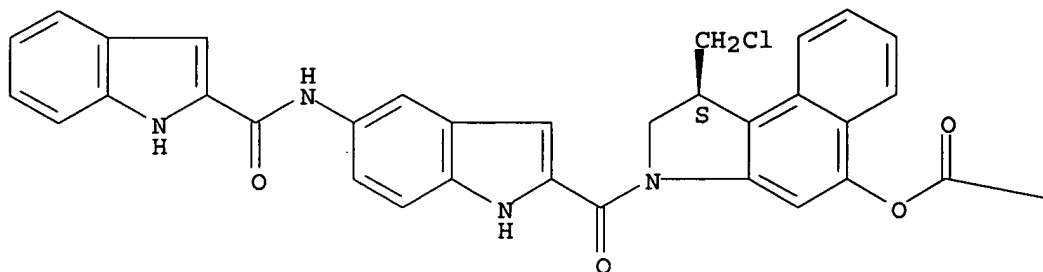
REFERENCE 1: 131:237670

L26 ANSWER 68 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 244154-63-0 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-[[[(methyamino)carbonyl]oxy]-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C33 H26 Cl N5 O4

SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER
 DT.CA Caplus document type: Journal
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry. Rotation (+).

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NHMe

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

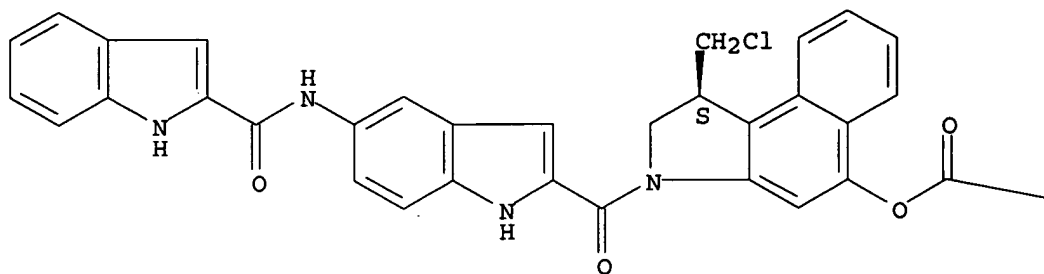
1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:237670

L26 ANSWER 69 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 244154-62-9 REGISTRY
 CN 1H-Indole-2-carboxamide, N-[2-[[[(1S)-1-(chloromethyl)-1,2-dihydro-5-
 [[(phenylamino)carbonyl]oxy]-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-
 (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C38 H28 Cl N5 O4
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER
 DT.CA Caplus document type: Journal
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B

—NHPh

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

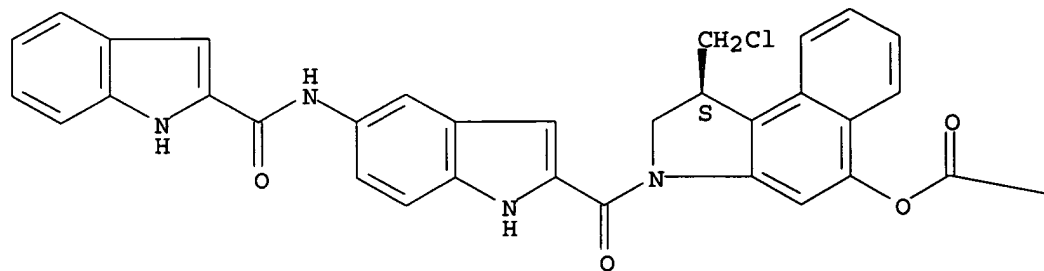
- 1 REFERENCES IN FILE CA (1907 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:237670

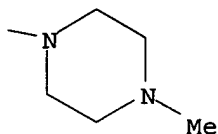
L26 ANSWER 70 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 244154-61-8 REGISTRY
CN 1-Piperazinecarboxylic acid, 4-methyl-, (1S)-1-(chloromethyl)-2,3-dihydro-
3-[[5-[(1H-indol-2-ylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-1H-
benz[e]indol-5-yl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C37 H33 Cl N6 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA Caplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry. Rotation (+).

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:237670

L26 ANSWER 71 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 244154-60-7 REGISTRY

CN Carbamic acid, dimethyl-, (1S)-1-(chloromethyl)-2,3-dihydro-3-[[5-[(1H-indol-2-ylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-1H-benz[e]indol-5-yl ester (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C34 H28 Cl N5 O4

SR CA

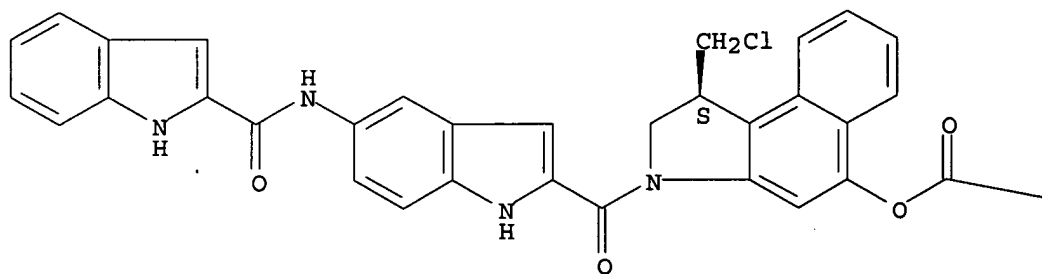
LC STN Files: CA, CAPLUS, TOXCENTER

DT.CA Caplus document type: Journal

RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry. Rotation (+).

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NMe2

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

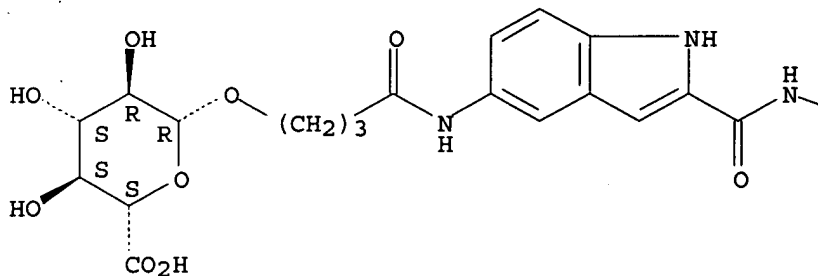
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REFERENCE 1: 131:237670

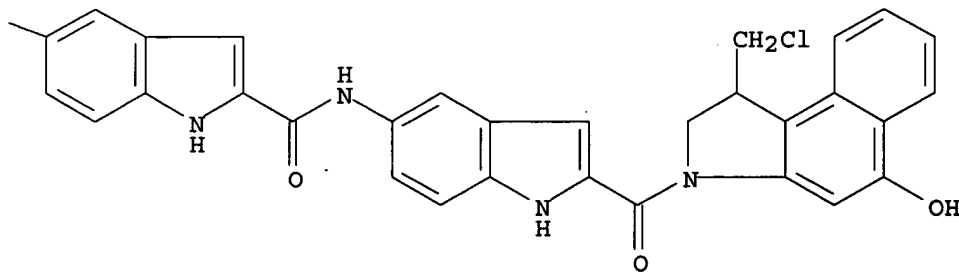
L26 ANSWER 72 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 199806-65-0 REGISTRY
 CN β -D-Glucopyranosiduronic acid, 4-[[2-[[[2-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]amino]-4-oxobutyl (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C50 H44 Cl N7 O12
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
 DT.CA Caplus document type: Patent
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

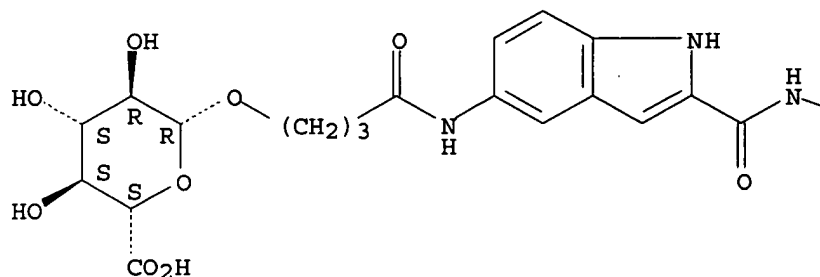
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REFERENCE 1: 128:48468

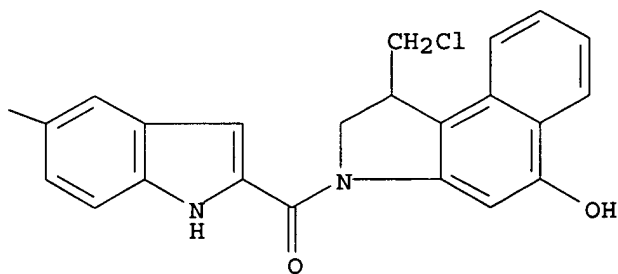
L26 ANSWER 73 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 199806-64-9 REGISTRY
CN β -D-Glucopyranosiduronic acid, 4-[[2-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]amino]-4-oxobutyl (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C41 H38 Cl N5 O11
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA Caplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

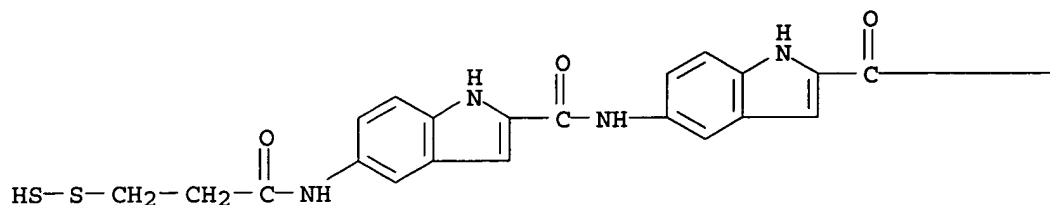
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REFERENCE 1: 128:48468

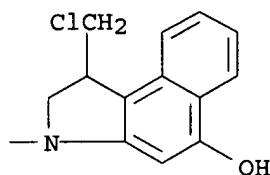
L26 ANSWER 74 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 199806-62-7 REGISTRY
CN 1-Propanesulfenothioic acid, 3-[[2-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]amino]-3-oxo- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C34 H28 Cl N5 O4 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

DT.CA CAPlus document type: Patent
 RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

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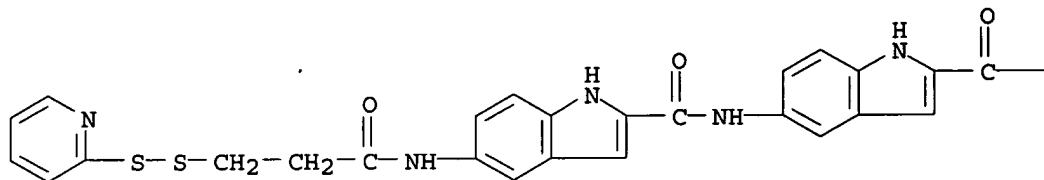
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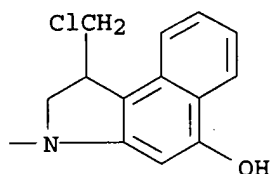
REFERENCE 1: 128:48468

L26 ANSWER 75 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 199806-61-6 REGISTRY
 CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-5-[[1-oxo-3-(2-pyridinyldithio)propyl]amino]- (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C39 H31 Cl N6 O4 S2
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
 DT.CA CAPlus document type: Patent
 RLD.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 128:48468

L26 ANSWER 76 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 199806-42-3 REGISTRY

CN β -D-Glucopyranosiduronic acid, 4-[[[2-[[[2-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]amino]-4-oxobutyl, methyl ester, 2,3,4-triacetate (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C57 H52 Cl N7 O15

SR CA

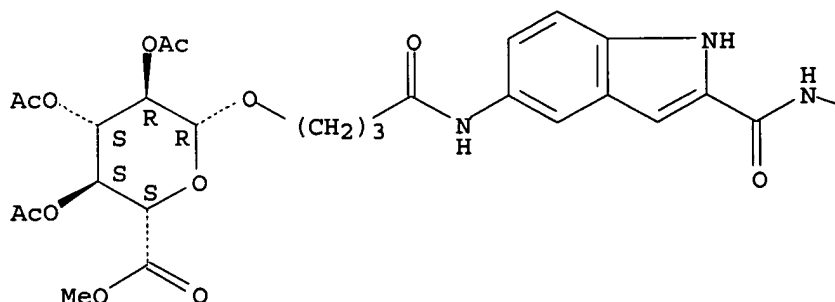
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

DT.CA Caplus document type: Patent

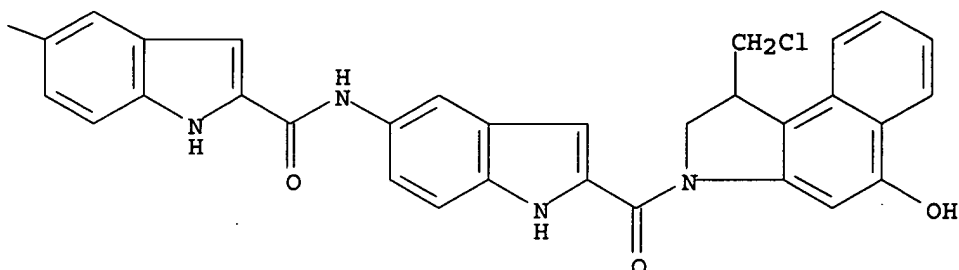
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 128:48468

L26 ANSWER 77 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 199806-41-2 REGISTRY

CN β -D-Glucopyranosiduronic acid, 4-[[[2-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]amino]-4-oxobutyl, methyl ester, 2,3,4-triacetate (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C48 H46 Cl N5 O14

SR CA

LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

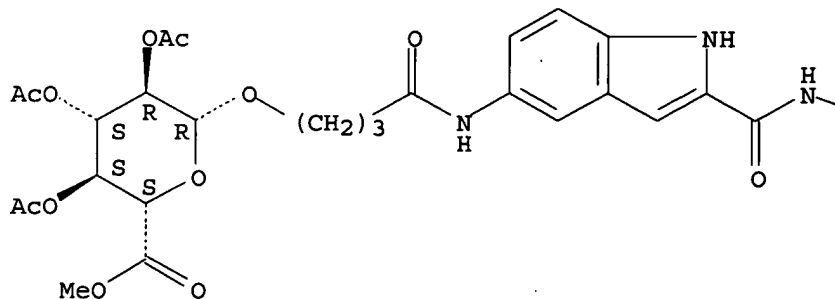
DT.CA Caplus document type: Journal; Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

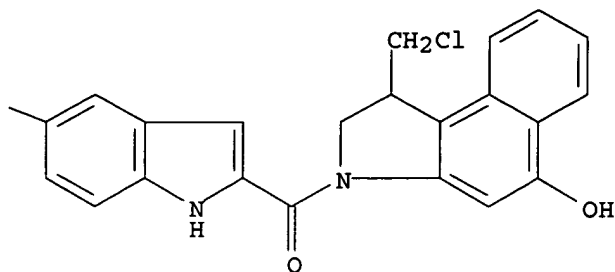
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)

2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:127387

REFERENCE 2: 128:48468

L26 ANSWER 78 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 199806-39-8 REGISTRY

CN 1H-Indole-2-carboxamide, N-[2-[[[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-1H-indol-5-yl]-5-[(4-hydroxy-1-oxobutyl)amino]- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C44 H36 Cl N7 O6

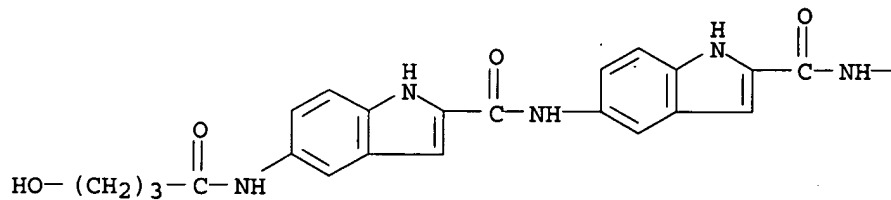
SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

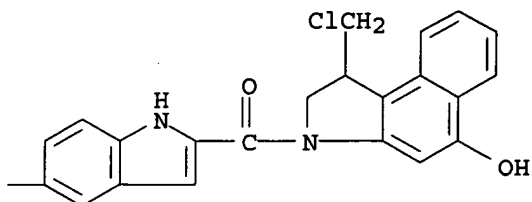
DT.CA Caplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

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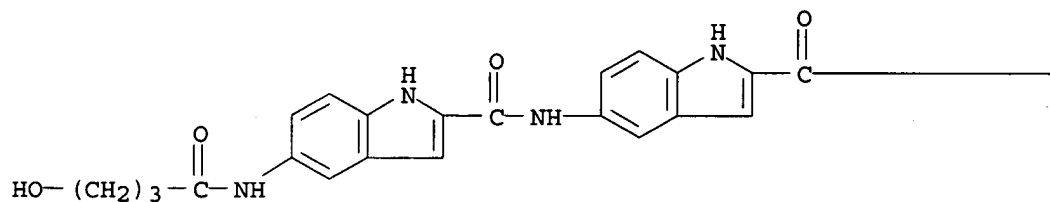
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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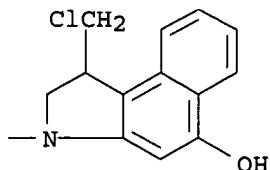
REFERENCE 1: 128:48468

L26 ANSWER 79 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 199806-38-7 REGISTRY
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 FS 3D CONCORD
 MF C35 H30 Cl N5 O5
 SR CA
 LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL
 DT.CA Caplus document type: Journal; Patent
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

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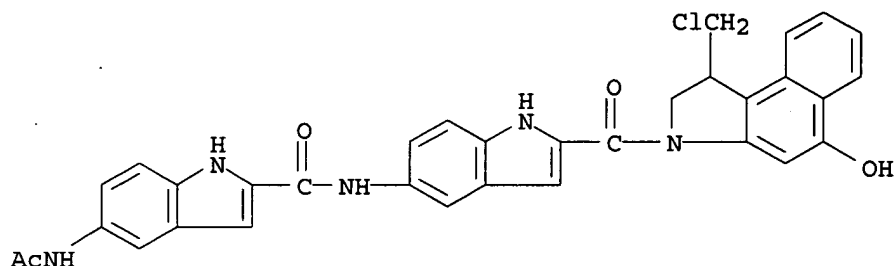
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:127387

REFERENCE 2: 128:48468

L26 ANSWER 80 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 199806-33-2 REGISTRY
CN 1H-Indole-2-carboxamide, 5-(acetylamino)-N-[2-[[1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]- (9CI)
(CA INDEX NAME)
FS 3D CONCORD
MF C33 H26 Cl N5 O4
SR CA
LC STN Files: CA, CAPLUS, PROUSDDR, SYNTHLINE, TOXCENTER, USPATFULL
DT.CA Caplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

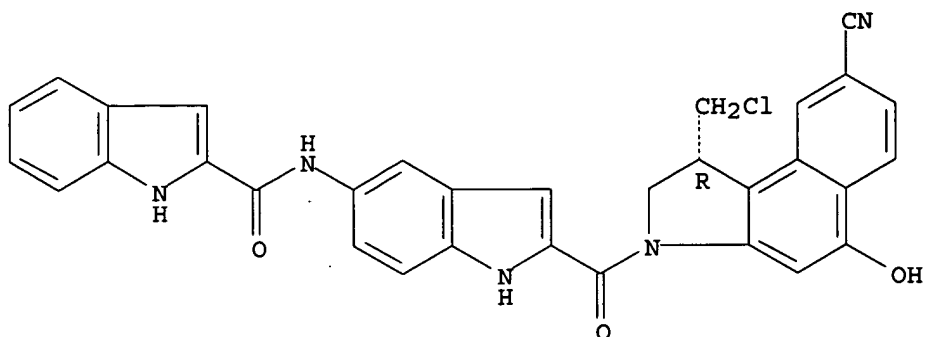
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REFERENCE 2: 132:321743

REFERENCE 3: 128:48468

L26 ANSWER 81 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
RN 178877-34-4 REGISTRY
CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-8-cyano-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-, (R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H22 Cl N5 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA Caplus document type: Journal; Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 128:61379

REFERENCE 2: 125:114357

L26 ANSWER 82 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN

RN 178877-33-3 REGISTRY

CN 1H-Indole-2-carboxamide, N-[2-[[1-(chloromethyl)-8-cyano-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-1H-indol-5-yl]-, (S)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C32 H22 Cl N5 O3

SR CA

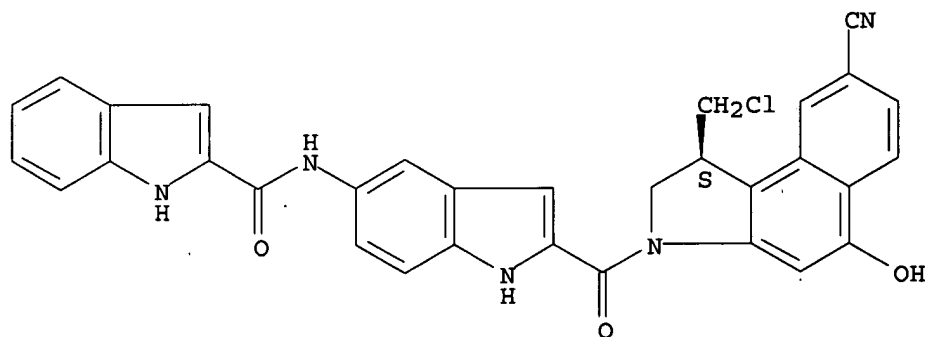
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

DT.CA Caplus document type: Journal; Patent

RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry. Rotation (+).



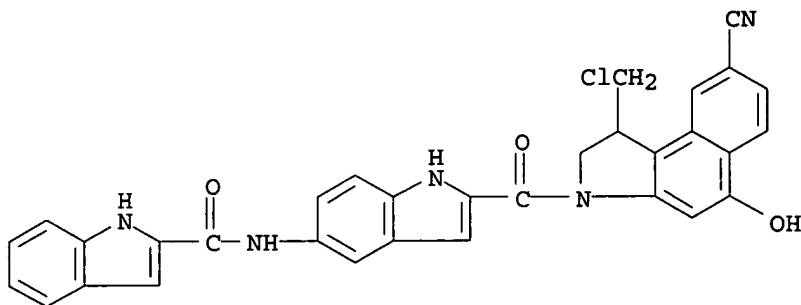
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2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 128:61379

REFERENCE 2: 125:114357

L26 ANSWER 83 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 178877-22-0 REGISTRY
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 FS 3D CONCORD
 MF C32 H22 Cl N5 O3
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER
 DT.CA Caplus document type: Journal
 RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 125:114357

L26 ANSWER 84 OF 89 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 173483-79-9 REGISTRY
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 FS STEREOSEARCH
 MF C32 H25 Cl N4 O4
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER
 DT.CA Caplus document type: Journal
 RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry. Rotation (-).

